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THE EXPERIMENTAL PRODUCTION OF ABSCESS OF THE LUNG *

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CLEVELAND

It is my intention to bring together here experimental data concerning the etiology of pulmonary abscess. There is no field in medicine which shows such active growth and so much varied and intensive investigation as that having to do with conditions in the thorax, and within this domain the question of pulmonary suppuration has had its full share of study. Moreover, the information now available in this restricted field carries a great lesson in prophylaxis, a part of one's professional duties that is becoming increasingly important. Thus, though it cannot be claimed that abscess of the lung is a common clinical entity, the lesson which may be indicated by determining its mode of occurrence has a wide application.

My interest and that of my associates in abscess of the lung developed from a study of the larger topic of postoperative pulmonary complications. Historical studies and six years of diligent and critical analysis of these disastrous surgical sequelae led us to believe that a common etiologic factor was present in the majority of these conditions, whether they were severe and immediately fatal sequelae, as in massive postoperative pulmonary embolism, or whether they were nonserious, fleeting and infrequently noticed sequelae. These studies led us to believe that embolism was a frequent factor in initiating the clinical disorder. A careful analysis of the conditions that surround all operations led to the belief that the source of postoperative complications must be the wound, which is the only condition common to all surgical procedures. Chilling, the seasonal incidence of pulmonary infection, the type and the duration of the anesthesia, the position of the patient were, after all, constantly shifting environmental affairs, which could not be even suggested as factors in many cases, because they were not present. As to the only common factor, the wound, it would appear that thrombosis was always present to a varying degree

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and that embolism might occur in any case. Obviously, the amount of trauma, the amount of infection, the mobility of the part and the occurrence of valves in the veins would play an important rôle in the size, number and dissemination of thrombi. The size of the embolus, the resistance and the condition of the host and the infectivity of the clot seemed to dictate the actual clinical picture. Such a hypothesis seemed open to experimental proof.

Abscess of the lung was chosen as our direct goal since it appeared that visible, tangible and more easily transmitted proof of the result might be obtained with this special postoperative pulmonary complication than with any other form of postoperative pulmonary complication. Laboratory investigations lasting throughout the past four years have led us down many blank byways but have given certain results that have already been substantiated by other investigators. These studies have shown that by the use of infected emboli, abscess of the lung may be created in the dog with great regularity. Moreover, the type and the duration of these intrapulmonic suppurative lesions have been shown to depend to a large extent on (1) the balancing of the immunity of the host and the virulence of the infecting organism and on (2) the actual type and class of the organism used to infect the embolus.

These studies concern the postoperative type of abscess of the lung, though their full significance may have a larger application. What I shall have to say, therefore, is especially restricted to abscesses of postoperative or post-traumatic origin. I include trauma, since under this form of injury the same vascular changes may be induced as in operations.

Previous studies have already indicated that about 30 per cent of all reported cases of pulmonary abscesses fall within this category. Little is known concerning the postpneumonic abscess, but I have long had in mind that if our contention concerning the vascular, embolic origin of the postoperative type is accepted, the postpneumonic type may be assumed to have its origin in similar basic conditions. It may be that pulmonary thrombosis with its resultant devitalization of the parenchyma of the lung is the forerunner of the postpneumonic abscess.

All must agree that the thorax has been the chief field of investigation since the war. This is, in part, due to its recent entrance into the domain of surgical endeavor, but it is more largely due to a better understanding of intrathoracic physiology, so greatly augmented by the imperative procedures of military surgery. At the same time, the great advance in roentgenologic technic through the use of substances impervious to the x-rays has been a direct stimulus. Finally, the creation of the youngest surgical specialty, bronchoscopy, and its brilliant diagnostic and therapeutic results have been a tremendous stimulus.

In the narrow field of abscess of the lung, the yearly increment to knowledge, both clinical and experimental, is stupendous.

In spite of all this work, one still finds no agreement concerning the important question of the etiology of pulmonary abscess. The two divergent views as to the mechanism that leads to the production of abscess of the lung, (1) that it is aspiration and (2) that it is embolism, remain. It is probable that much truth resides in each view; that, indeed, both mechanisms are present in all cases of chronic pulmonary abscess. My associates and I have been driven by experimental evidence to this point of view, and it is our hope that by the recital of both laboratory and clinical evidence we may be able to lend some weight to this thought.

Let me examine for a moment the aspiration theory. Those who hold this view that infected material aspirated during an operation is the cause of abscess of the lung, as well as of other postoperative pulmonary complications, have brought forward to support their contention the following data:

Material in the mouth is aspirated during operations. This was long ago shown by Hoelscher and Kelly, and recently by Corper and Lemon. Hoelscher placed a dye in the mouths of animals and after anesthesia found the dye in the lungs. Lemon utilized a barium suspension, with the same results. More recently, Iglauer carefully studied the larynx and trachea after tonsillectomy and found blood in the trachea in about 40 per cent of all cases in which local anesthesia was used. Ochsner and Nesbit made similar observations. Myerson and the Dailys found this condition in about 75 per cent of tonsillectomies in which general anesthesia was used. There can be no doubt that a part of the buccal contents is, under anesthetic conditions, aspirated into the tracheobronchial tree and even into the lung. But even under nonanesthetic conditions, if the animals are kept in a vertical position, a certain amount of buccal contents is normally aspirated.

Certain limited experimental data are on record that demonstrate the production of an infection in the lung by insufflation and transbronchial implantation. Blake and Cecil claimed to have produced pneumonia in monkeys by intratracheal insufflation, but it should be noted that they injected the organisms with a syringe and needle between rings of the trachea, which is scarcely the same as simple insufflation. Meltzer used relatively enormous quantities of virulent pneumococci and yet produced pneumonia in only a small percentage of animals, and Winternitz not only used quantities of bacteria far out of proportion to what could occur in man, but further vitiated the possibility of applying his success in producing pneumonia in rabbits by forcing in under pressure through a catheter a large quantity of air immediately after the injection of the bacteria. Smith utilized a transtracheal injection in those animals in which he produced abscess

of the lung. This is of some significance, in view of the extremely rich venous and lymphatic plexus about the trachea. Indeed, Winternitz, himself, showed that if the tracheal wall was injured, bacteria passed down these channels and out into the lung, where they produced pneumonia. Moreover, Smith did not succeed when he used dogs. Crowe and Scarff utilized a pledget of cotton soaked in fresh scrapings form the teeth of patients with pyorrhea alveolaris, which they introduced deep into the bronchial tree with the bronchoscope. Only when such scrapings were used and the cotton pledget packed in tightly was abscess produced. When other organisms were introduced, abscess did not result. Complete blocking of the bronchus seemed of the greatest importance. The recent experiments of Pilot and Davis lend further weight to this theory. They produced abscesses in rabbits by the intratracheal injection of material containing fusospirochetes when iodized poppy seed oil 40 per cent was utilized on top of the insufflated material to trap it there. In the experiments conducted by Joannides and Hedblom, abscesses were produced by intratracheal insufflation of fusospirochetal material. The results were not uniform, there were many fatalities, some of the animals developed gangrene rather than abscess and the authors did not state their technic nor the quantity of material introduced.

I shall now take up the embolic theory. It has been already seen that aspiration is of frequent, if not universal, occurrence. Does that mean that there is any harm in it? The tracheobronchial defense is elaborate. The lining itself is of a protective nature; it is constantly exposed to infection. My bronchoscopic colleagues tell me that they have frequently removed teeth, bridge-work and other foreign bodies, resident in the bronchi for years, without the production of abscess, and when abscess is produced it is a bronchiectatic not a parenchymatous abscess and is relieved by removal of the foreign body in about 95 per cent of the reported cases. I have known a patient with carcinoma of the esophagus in whom an opening developed between a bronchus and the esophagus below the constriction so that for over a month he vomited gastric contents (the patient being fed by a gastrostomy opening) via his right lung. At autopsy the lung was normal.

There is much experimental evidence to support the contention of high endobronchial resistance. Hundreds of investigators have attempted the study of pneumonia and tuberculosis by insufflation methods. These experiments are still so inconclusive that serious doubts may be held as to whether or not these diseases are chiefly air-borne. In the narrow field of pulmonary suppuration there have been many more failures than successes and the fact that we, too, have failed to produce abscess by insufflation and endobronchial insufflation merely leaves us with the majority of investigators.

As to pulmonary complications as a whole, ever since the first papers of Mikulicz and Kausch describing postoperative pneumonia with local anesthesia, there has been abundant evidence that irritation from an inhalation anesthetic is not a chief cause. It is known, too, that these postoperative sequelae arise most frequently in relation to epigastric operations. Competent studies have shown that though in general the incidence of postoperative complications is 3 per cent, in operations in the epigastrium it is from 8 to 10 per cent. Some have felt that this was due to the greater mobility of the part, since postoperative pulmonary complications are extremely rare following intracranial procedures or orthopedic procedures in which the part is well splinted. It may be further stated that operations on the extremities disclose that the body is protected from embolism by the valves in the peripheral veins, a protection which is wanting in the abdominal and thoracic cavities and in the neck. Moreover, tonsillectomy is a chief source of abscess of the lung. As a matter of fact, tonsillectomy constitutes almost 50 per cent of the surgical procedures in a septic or potentially septic field, and post-tonsillectomy abscess constitutes about 50 per cent of postoperative abscesses. It seems that the potentially septic field may be the more important factor and certainly it is under this condition that the greater percentage of the postoperative pulmonary complications arise. Some have felt that a seasonal incidence occurred and that the percentage of postoperative pulmonary complications fluctuated with the seasonal incidence of pulmonary disease. This has not been a striking observation in our experience. In three separate studies in two hospitals, the incidence of postoperative pulmonary complications did not reveal an increase in the percentage of these sequelae comparable to the normal fluctuation of respiratory disease. Moreover, is it not true (1) that there has been a great effort to clean up the buccal cavity before anesthesia and (2) that inhalation anesthesia is now administered with a greatly perfected technic? Yet postoperative pulmonary complications, as a whole, and pulmonary abscess, in particular, continue unabated. Those surgeons, such as Crowe, who lean toward the aspiration theory cite absence of such complications in their cases as due to care in protecting their patients from aspiration, but do they give themselves credit for their excellent surgical technic? Such surgeons speak of delicacy in handling tissue and the careful ligation of all blood vessels, precautions that guard against thrombosis and embolism.

In this attempt to discuss the two opposing theories—of aspiration and of embolism—I do not expect to do more than stimulate interest and show how there may be good reasons for supporting either contention. The critical, painstaking and long continued studies of Professor Whipple have shed great light on this important matter. He is

doubtless the best informed proponent of the aspiration theory. His colleagues and pupils will, I hope, agree at least with that part of our experimental work which seems, in its present phase, to need a union of both the aspiration and the embolism mechanisms for its explanation. It is in relation to the chief factor of chronicity of the pulmonary abscess that I refer.

With this introduction, I shall now attempt to review the main stages in our work of the past four years, work for which the successive fellows in charge of our surgical laboratory deserve chief credit: Dr. Schlueter, Dr. Holloway, Dr. Herrmann and Dr. Cox.

EXPERIMENTS

With this background, it was wisest to commence with attempts to produce pulmonary suppuration by aspiration. For six months, experiments were carried out in which we insufflated via a bronchoscope to all parts of the lungs of dogs infected material of all sorts, utilizing all the common bacteria, with and without organic or inorganic foreign bodies, and with and without injury to the mucous membrane of the bronchus. Bacteria were blown in, and were placed in meat, tonsils and nuts and these firmly placed in the deepest portions of the lungs. In no case was a definite abscess produced. This agreed with the work of previous investigators and with much that has been attempted since. Dr. Crowe spoke of two years of unsuccessful attempts until scrapings from teeth were used; Allen recorded many attempts that were unsuccessful until complete blocking of the bronchus was definitely established; Smith had no success in dogs. Even those who had success had more failures than abscesses unless, as in the experiments of Kline or Allen, such large amounts were introduced that little analogy could be had to the condition in man. Moreover, in these latter instances, the lesion produced resembled gangrene more than abscess.

Fortified by these failures we initiated experiments utilizing an infected embolus. The setting free in the venous circulation of infected, artificial clots led frequently to diffuse and fatal lesions. Therefore, to control the spread of infection better and to encourage a walling off process, artificial emboli were constructed by utilizing a small excised segment of vein tied off at both ends and filled with the desired bacteria. When the condition of a sufficiently virulent organism was achieved, success in producing walled off abscess of the lung resulted in about 90 per cent of the attempts. Such abscesses reached maximal size and intensity within from ten to fourteen days, and the majority went on through healing by fibrosis until in from three to three and a half weeks no sign of activity or abscess remained. In a few instances, because of too great a discrepancy between the virulence of the organism and the resistance of the host, the abscess enlarged, broke into

the pleural space and killed the animal. More rarely, the lesion spread rapidly and a general pneumonitis resulted in death before the production of a typical abscess. By lobectomy or autopsy, a great number of such abscesses were studied histologically, and it was clear that we were dealing with parenchymatous lesions that at first were not in connection with the bronchial tree.

The rare failures in this series of experiments emphasized the value of the immunologic relations and gave us the hope that, when these

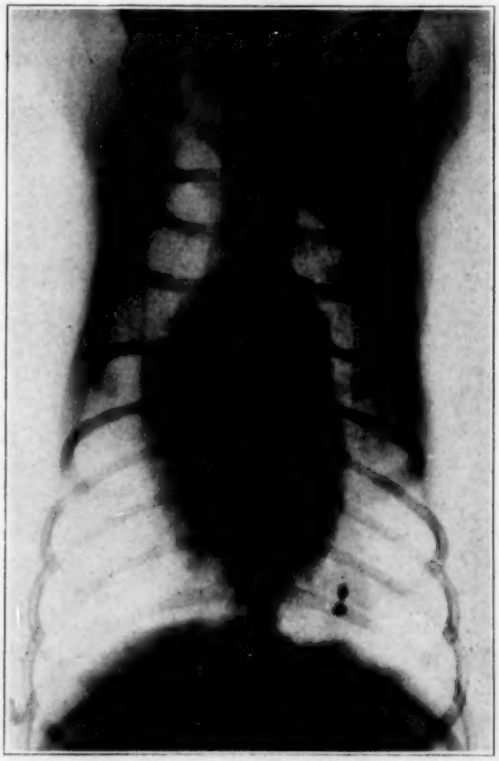

Fig. 1 (dog Y 10).—This and following illustrations of experiments in which infected emboli were freed into the jugular vein are typical of the whole series from which they have been selected. Here an embolus of muscle infected with a pure culture of Staphylococcus aureus was freed into the jugular vein. The roentgenogram, taken three days after embolism, shows some density about the foreign body.

factors were correctly balanced, even free infected clots might result in abscess. With this in mind, two sets of experiments were set up. In the first group, the immunity of the animal was increased by previous immunization with the organism later to be used in the clot. Immunization was carried to various stages, and the experiment was further

controlled by the use of normal animals in the complete experiment. Clots infected with the organism previously used to immunize the animals were made in vitro, and then equal amounts of this were freed into the jugular veins of the immunized animals and into the vein of a control animal. In these experiments, the pulmonary lesion varied with the resistance of the host. In highly immunized animals, a transient reaction of from twenty-four to forty-eight hours occurred; in partially immunized animals, abscess resulted, and in the non-

Fig. 2 (dog Y 10).—A roentgenogram, taken five days after embolism, shows an increasing area of density with an area of rarefaction in the center.

immunized control animals, death resulted from a rapidly spreading pneumonitis. Thus encouraged, we attempted to reproduce in the animal more nearly the condition that might be found in human beings; i. e., we attempted to make the dog manufacture his own infected clot. To do this, the jugular vein was exposed, traumatized and ligated proximal to the injured area. Bacteria were then injected in and about the vein. At varying intervals later on, the wound was opened and the clot excised and freed into the opposite jugular vein. In these

experiments, abscess resulted, unless the clot had been too long resident in the vein. Control experiments showed a rapid attenuation of the virulence of the organism in these clots, and after seventy-two hours such clots failed to produce abscesses.

The experiments thus far dealt largely with our ability to produce in animals, with the use of infected emboli, walled off parenchymatous pulmonary abscesses. By a study of the immunologic factors involved,

Fig. 3 (dog Y 13).—Two emboli were freed into the jugular vein: (1) an embolus of potato infected with Staphylococcus aureus, and (2) an embolus consisting of a lead shot containing a cavity in which a plug of muscle infected with Staphylococcus was placed. The specimen, fourteen days after embolism, shows two abscesses in the left lower lobe.

we had been able to escape from the obvious criticism attached to the early experiments that a false organic capsule had been used, which, though autogenous, was not comparable to a simple infected clot. The results obtained in the latter experiments were encouraging, but we were still confronted with the fact that our experimental lesions all

tended to heal within four weeks and thus were not comparable with abscess of the lung in man, which is characterized by its chronicity.

A careful survey of the published work, as well as a careful revaluation of our own work, seemed to point to two possible factors that might play a rôle in determining the duration of the lesion. One was the physical problem, the matter of cough and the horizontal plane of the dog's tracheobronchial tree; the other was the part played by specific organisms. We were influenced to study the effect of coughing

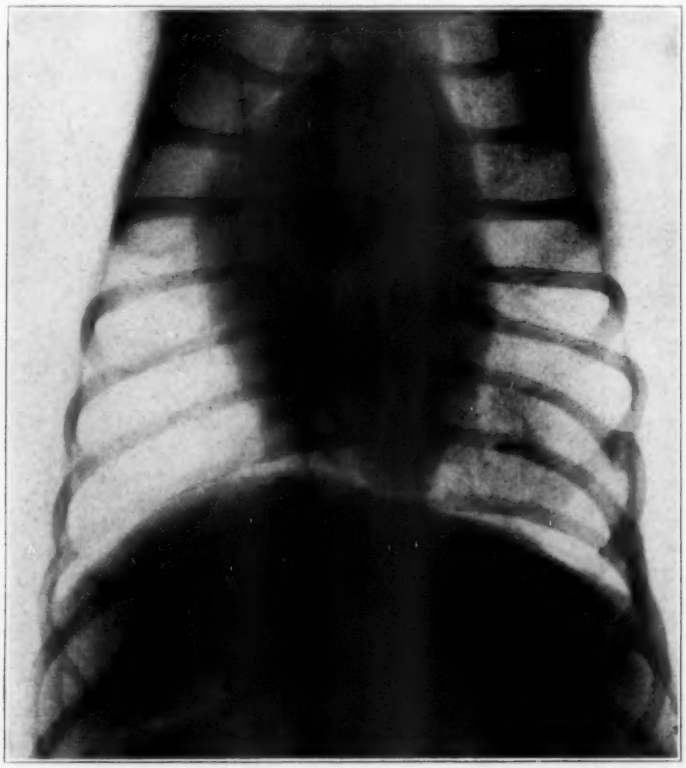

Fig. 4 (dog Y 38).—An embolus of vein-segment filled with blood infected with Bacillus coli, Staphylococcus aureus and Pneumococcus type II. The roentgenogram, taken five days after embolism, shows an area of infiltration in the left lower lobe.

from a study of the experiments of Van Allen and of Brown and Archibald, who had shown that when coughing is induced, the intrabronchial pressure is increased and any material within the lung is blown farther into the peripheral pulmonary ramifications. To test this, Dr. Herrmann produced abscesses after the original method using as embolus an infected segment of a vein, and when these were well

established, he placed the animals three times a day for from three to fifteen minutes in a chamber containing chlorine gas in the proportion of 1 part to 3,000. This irritant produced excessive coughing. Studies in this group of experiments showed that the abscesses greatly increased in size and remained active for a period of from four to five weeks. The amount of coughing necessary to bring this about seemed entirely out of proportion to what occurs in human beings, and further work was abandoned as not bearing directly on the solution of the problem.

We were then ready to take up the rôle of the organisms of the mouth, especially the spirochete and the fusiform bacillus. This was

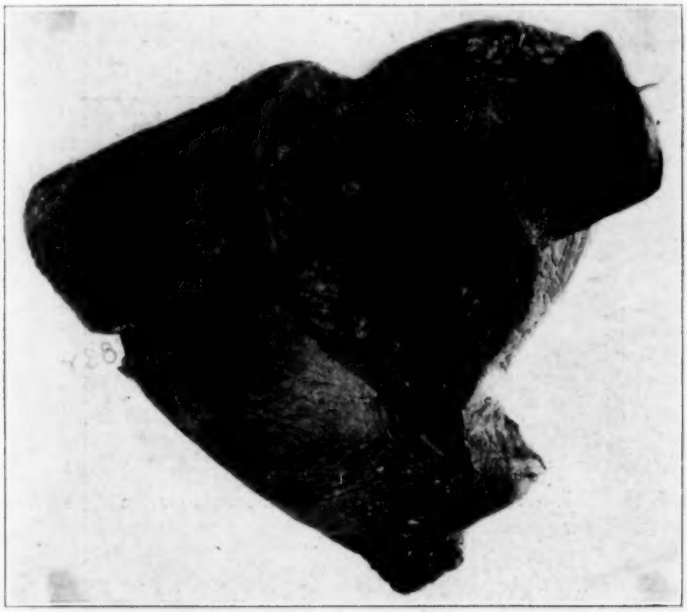

Fig. 5 (dog Y 38).—A specimen, sixteen days after embolism, showing a small abscess cavity.

not done earlier because we had always considered these organisms as secondary invaders, more or less saprophytic, and also because if embolism is a chief factor in the production of pulmonary abscess, these organisms could account only for abscesses secondary to operations about the mouth and the nasal sinuses. The experiments of Kline, Smith, Crowe and others had clearly established the important relationship of this group of organisms. The use of arsenical drugs therapeutically in cases of abscess of the lung had long been shown to have specific value, although alone they could not effect cures, and pathologic and bacterial studies both in this entity and in the allied condition of pulmonary gangrene had shown some definite relationship.

A large number of insufflation experiments and intrabronchial bronchoscopic placements were performed with material swarming with spirochetes and freshly obtained from the gum margins of a patient with pyorrhea alveolaris. No insufflation experiments gave results and only in one case, in which an inverted skin clip was firmly engaged and remained in the bronchial wall, was an abscess produced. This proved to be a bronchiectatic cavity when the dog was killed on the seventy-fourth day. Repetition of the experiment devised by Crowe and Scarff of creating a suppurative frontal sinusitis with the spirochete and allied organisms of the gums yielded no results. It appeared increasingly obvious that the success of others depended on complete bronchial obstruction, a phenomenon that we felt was not probable in human beings.

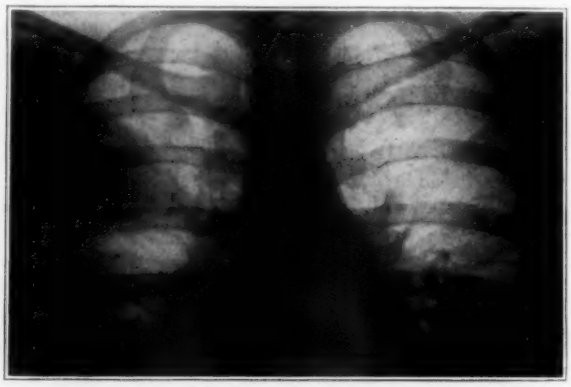

Fig. 6 (L. M.).—A roentgenogram of the thorax fourteen days after cholecystectomy, showing a small abscess.

Later still we carried out a series of experiments in which scrapings from the gum margins of a person with pyorrhea alveolaris were placed in a vein-segment embolus and the latter freed into the venous circulation. Abscesses were produced with almost universal regularity. Abscesses created by these organisms became really comparable with those in man, and one remained active for 101 days. Careful bacteriologic studies showed that we were utilizing a host of organisms both aerobic and anaerobic. In addition to the spirochetes and the fusiform bacilli there were motile and nonmotile organisms of many types.

Having satisfied ourselves that these anaerobic organisms have to do with the factor of chronicity in these experimentally produced abscesses, we once more attempted to bring the experiments into closer analogy with human conditions. Clots formed in test tubes were infected with the same material from gum margins, allowed to incubate and then freed into the venous circuit. Again abscesses were produced,

and these became chronic. In these experiments, matters of immunity could not be so well adjusted and thus in several cases there resulted rapidly spreading and fatal lesions, but typical abscesses were more common.

SUMMARY AND CONCLUSION

The translation of all this work and its applicability to the type of pulmonary abscess in human beings may seem confused. There are, however, certain landmarks so clearly demonstrated that we can now approach the solution with more confidence. 1. In our experience, the surest way to produce an experimental abscess is by the use of an infected embolus. If the immunity factors are controlled, free infected autogenous clots will give this result. 2. The insufflation and aspiration

Fig. 7 (L. M.).—A roentgenogram, thirty-five days after operation, showing that the lesion has disappeared.

of bacteria, anaerobic or aerobic, freshly obtained from the gums of persons with pyorrhea or from an abscess cavity, and even the mechanical placement by way of a bronchoscope of such bacteria and material, will not produce abscess of the lung unless there is complete bronchial obstruction, with subsequent atelectasis and anaerobiasis. 3. Aspiration of buccal contents is a usual occurrence in patients submitted to general anesthesia and is probably of frequent occurrence in conscious persons.

With these criteria we must deduce that the simple aspiration of buccal contents does little harm; yet in most cases of pulmonary abscess in human beings the mouth organisms are found. We propose that embolism from a septic field produces the original lesion and that it becomes a chronic abscess only when secondarily infected by the ever present mechanism of aspiration. It may even be that in operations about the mouth these anaerobic organisms are actually included

in the thrombi. This may indeed account for any discrepancy in favor of a higher incidence for abscess following tonsillectomy than following operations in septic fields elsewhere. Fetterolf and Fox beautifully demonstrated the thrombosis in the tonsillar bed after operation. The incidence of abscess after operation under local anesthesia suggests this possibility. These mouth anaerobes would tend to make for chronicity and thus impress the observer with the danger of operations on the tonsils. What may well occur is that frequently small abscesses are produced early in the postoperative period, and are called areas of local atelectasis, areas of infarction or bronchopneumonic patches, and these, unless secondarily infected with mouth organisms during the normal aspiration of buccal contents in sleep, heal within two or three weeks. I shall be able to show you exactly this occurrence in two cases, one following cholecystectomy and the other following otitis media with lateral sinus thrombosis. As but few spirochetes were found in the mouth of one of these patients and none in the other, we predicted, as in our dogs with abscess of simple pyogenic origin, that chronicity would not occur. The abscess in one of these cases healed within four weeks and that in the other had lost all signs of activity at the end of eight weeks, and gave promise of quiescence shortly. Probably many similar small abscesses occur and heal. They must be recognized in the first week or two. Many transient postoperative pulmonary complications may be potential abscesses.

It will, of course, have been noted where our experimental work now leads us. In order to duplicate the conditions in human beings, we must produce abscess of the lung experimentally, preferably by making an abscess about a large vein in an animal; by reoperation and trauma, we must give rise to a clot in that vein (preferably, perhaps, a pelvic vein and using common pyogenic organisms); this must dislodge and create an acute abscess in the lung; before this heals, we must by insufflation secondarily infect this cavity with organisms from the mouth. When this is done, we shall have reproduced what occurs in man.

This experiment has long been our ideal, but there are many difficulties. The relative immunity of the dog to man's organisms is well known, and the animal does not seem to have an equally effective variety of its own. Moreover, it is difficult to infect the acute abscess by insufflation from above, for it is a real parenchymatous lesion and does not always present a sufficient opening into the bronchus for the invasion with bacteria from above.

Finally, it must be borne in mind that the only factor common to all surgical procedures is the wound. Anesthesia and anesthetics vary, so do the position of the patient, the heat of the room and the incidence of seasonal respiratory disease. The wound, with injury to blood vessels

and all its perils, is the surgeon's task; he should look there first of all for ensuing difficulties and not to environmental conditions that are always shifting.

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DIGITALIS STUDIES ON CHILDREN WITH HEART DISEASE

THE EFFECTS OF DIGITALIS ON THE ELECTROCARDIOGRAMS OF CHILDREN WITH RHEUMATIC FEVER AND CHRONIC VALVULAR HEART DISEASE*

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The purpose of this study was to determine the effects of digitalis on the electrocardiograms of children with rheumatic heart disease and signs of heart failure. It has been shown by Cohn and his co-workers [1] that an alteration in the size, shape and direction of the T wave of the electrocardiogram is the earliest index of digitalis action. This may take place before disturbances in rhythm and conduction time have occurred and before the patient exhibits any minor toxic manifestations, such as nausea and vomiting. The changes in the electrocardiogram consist essentially in a progressive diminution of the size of the T wave in either one or all three leads, with final inversion of previously upright waves. In cases yielding downwardly directed T waves before the use of digitalis, the drug produces eventually upwardly directed waves. These variations have found ample support in subsequent clinical and experimental observations on both man and animals.[2] In children, however, a similar systematic study of the effects of digitalis on the electrocardiogram has not been carried out with any degree of accuracy. Since the optimal dosage of digitalis and its value and limitations in children with heart disease are still mooted questions,[3]

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1. Cohn, A. E.; Fraser, F. R., and Jamieson, R. A.: The Influence of Digitalis on the T. Wave of the Human Electrocardiogram, J. Exper. Med. **21**:593, 1915.

2. Robinson, G. C., and Wilson, F. N.: A Quantitative Study of the Effect of Digitalis on the Heart of the Cat, J. Pharmacol. & Exper. Therap. **10**:491, 1918. White, P. D., and Sattler, R. R.: Effects of Digitalis on the Normal Human Electrocardiogram, J. Exper. Med. **23**:613, 1916.

3. Eggleston, C.: The Dosage and Administration of Digitalis in Infancy and Childhood, read before the Fifth Avenue Hospital Association, Dec. 7, 1927.

it seemed important before proceeding with our studies of digitalis in such children to evaluate the changes produced by this drug on the electrocardiogram. This was of special interest to us since in recent years one of the methods used for the study of the dosage, the standardization, the rate of absorption and elimination and the maintenance dose of digitalis in man, has been based on the effects produced by this drug on the T wave of the electrocardiogram.[4]

The only observations that appear to have been made on the electrocardiograms of children following the administration of adequate doses of digitalis are those of McCullough and Rupe[5] and of Samet and Tezner.[6] Both these studies were concerned only with healthy children.

McCullough and Rupe administered a standardized tincture of digitalis having an activity of approximately 1 cc. per cat unit to a selected group of thirty-six children varying in age from 1 to 15 years, none of whom had any evidence of heart disease. Electrocardiograms were taken before and after the administration of the drug. All children received the complete course of digitalis within six days, and it was administered to all in a quantity that was sufficient to produce usually minor toxic manifestations, such as nausea and vomiting. Indeed, some of the children received from two to five times as much digitalis per pound of body weight as was necessary to produce an optimum therapeutic effect in adult patients with heart disease. Despite these large doses, in only four of the thirty-six children were any changes noted in the T wave, and these were an increased inversion in T 3 only. In three children a partial A-V block was noted, and in four there was a definite increase in the P-R interval, the highest reaching four-tenths seconds. The most significant changes recorded in the electrocardiograms seem to be what they considered a "persistent decrease in the ventricular rate" of at least 15 or more beats per minute. (No mention is made of how long this slowing persisted.) They also considered an exaggerated sinus arrhythmia to be the most common change following the use of digitalis. In one child sino-auricular block appeared during the course of medication. No effects were observed in ten children.

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4. Pardee, H. E. B.: Notes on Digitalis Medication: I. The Rate of Disappearance of Digitalis from the Body. II. Therapeutic Dose of Tincture of Digitalis, J. A. M. A. **73**:1822 (Dec. 13) 1919; Rate of Absorption of Digitalis from Gastro-Intestinal Tract, ibid. **75**:1258 (Nov. 6) 1920. Bromer, A. W., and Blumgart, H. L.: The Maintenance Dose of Digitalis: An Electrocardiographic Study, J. A. M. A. **92**:204 (Jan. 19) 1929.

5. McCullogh, H., and Rupe, W. A.: Studies on the Dosage of Digitalis in Children, Am. J. M. Sc. **162**:231, 1921.

6. Samet, B., and Tezner, O.: Ueber Digitalis Wirkung bei Gesunden und Kranken ohne Herzinsuffizienz, Monatschr. f. Kinderh. **31**:300, 1925.

Samet and Tezner claimed that they were unable to note any regular changes in the T wave in their series of children. In some cases they did find a slight reduction in the size of the T wave after the administration of digitalis (the amounts are not stated), but these changes varied markedly in different children. In some cases they saw no changes, yet in others the T wave appeared larger after the use of the drug than prior to its administration; such alterations were particularly noticeable at a time when other toxic manifestations were definitely present. Sinus arrhythmia with marked slowing was a rare observation. They recorded dropped beats and sino-auricular block, but extra systoles were not seen in any of their records. Unfortunately, their report lacks adequate data on the number of children studied and the exact dosage of digitalis given each child.

DETAILS OF THE EXPERIMENT

A body-weight (1.5 mm. of the drug per pound of body weight) of a standardized tincture of digitalis, having an activity of approximately 1 cc. per cat unit, was administered to twenty-four children. There were eleven boys and thirteen girls, the youngest being 4½ and the eldest 15 years.

All the children were admitted to the Montefiore Hospital within the past three years, and in each instance there was a definite history of recurrences and exacerbations of rheumatic fever. All showed definite organic valvular involvement of the heart, and symptoms and signs of progressive heart failure.

Eighteen of the children had sinus rhythm with a ventricular rate that varied from 70 to 120 beats per minute. One child had a sinus bradycardia with a ventricular rate of 50, and five children showed auricular fibrillation of the chronic or permanent form. The ventricular rates of the latter varied, depending on the degree of activity of the disease which the children presented.

Careful attention was paid so that these children would not receive any drug within the six weeks preceding the tests. The digitalis was given in one dose to each child at 9 a. m. The children with auricular fibrillation received the drug at 10 a. m. Each child had a single control electrocardiogram taken preceding the administration of the drug, and, in addition, ten of the children had control electrocardiograms taken daily at approximately the same time on each of five consecutive days in order to determine whether the T wave showed variations from day to day before any medication was taken.

In four children the experiments were repeated several months apart in order to test the effect of digitalis in the same child, during both the active stage and the so-called inactive stage of rheumatic fever. Similar experiments were repeated in three children in whom no effects were observed in the electrocardiograms following the first test.

Before reviewing the results obtained in these tests it may be worth while to consider the usual electrocardiograms seen in children with rheumatic fever and heart failure with special reference to that portion of the electrocardiogram with which we are concerned in these studies, namely, the S-T interval and the T wave.

The S-T Interval in Children with Rheumatic Fever.—Within recent years attention has been called to various changes produced by rheumatic fever on this portion of the electrocardiogram in adults with this disease. In a series of sixty-five patients with rheumatic fever, Rothschild, Sacks and Libman [7] noted alterations in the R-T or the S-T segment either alone or in combination in 45 per cent of their cases. Children were not included in their observations.[8] These authors claimed that characteristic changes of this segment proved more frequent in rheumatic fever than in any other febrile condition.

Normally, the first part of the ascending and descending limbs of the R wave of the electrocardiogram lies approximately at the same level. After the downstroke of the R wave reaches the base line there follows a short interval before the T wave begins during which the galvanometric string either is quiescent or records a slow rise in the curve. This segment is the R-T period or, when the S wave is present, the S-T period.

One of the significant deviations is that which occurs when the downstroke of the R wave fails to reach the base line and initiates an upward curve occupying the whole of the R.T period which becomes incorporated in the upstroke of the T wave so that it appears that the latter is given off directly from the R wave.

Since the S-T or the R-T segment form an important part of our studies in the alterations produced by digitalis on the electrocardiogram, we have studied this portion of the curve in a large series of children with rheumatic fever.[9] If it is true that this portion of the electrocardiogram is affected by rheumatic fever in at least 45 per cent of adults, similar changes, if present in children, might alter our interpretation of the effects of digitalis on the S-T segment [10] and the T wave of the electrocardiogram.

In eighty-seven children with rheumatic heart disease during both the active and the inactive phase of the disease, the average duration of the S-T interval was found to be 0.117 seconds in lead I, 0.113 seconds in lead II, and 0.119 seconds in lead III. Lincoln and Nicolson [11] stated that because the T wave of the electrocardiogram in normal children whom they studied arose frequently from the R or the S wave, they were unable to measure the S-T transition in their records.

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7. Rothschild, M. A.; Sacks, B., and Libman, E.: The Disturbances of the Cardiac Mechanism in Subacute Bacterial Endocarditis and Rheumatic Fever, Am. Heart. J. **2**:356, 1927.

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9. Weiss, M., and Schwartz, S. P.: The Electrocardiogram in Children with Chronic Rheumatic Valvular Heart Disease and Heart Failure, unpublished observations.

10. Pardee (footnote 4, second reference).

11. Lincoln, E. M., and Nicolson, G. H. B.: The Hearts of Normal Children: Electrocardiographic Records, Am. J. Dis. Child. **35**:1001 (June) 1928.

While we were occasionally unable to measure this interval in one lead or more rarely in two leads, it was only in about 10 per cent of the cases that there was no measurable interval in all three leads.

In only seven instances was the S-T interval above the iso-electric line, and since this was noted also in normal children we believe that it is of no significance in children with rheumatic fever. Consequently, this change need not be considered in studying the effects of digitalis on the S-T interval.

The T Wave in Children with Rheumatic Fever.—The T wave in children with rheumatic fever and organic valvular involvement of the heart, during both the active and the inactive phase of the disease, does not differ in size, shape or form from the similiar deflection in children with normal hearts.[12] The average height and range is the same. The wave is highest in lead II and lowest in lead III. In a group of eighty-seven children with chronic valvular heart disease who were studied with electrocardiograms in the wards of the Montefiore Hospital for a long period, there was no progressive increase in the size of the T wave with age. On the contrary, in several of these children between the ages of 10 and 15 a definite decrease in the size of the T wave was noted, when comparisons were made with records taken one or two years apart.

T 3 was inverted in 33 per cent of cases studied by us.[9] This is approximately the same percentage found in a group of normal children observed by Lincoln and Nicolson.[11] In two of our children there was combined inversion in leads II and III. Inversion of the T wave does not normally occur in these leads, and we can offer no explanation for its presence in these children. In two instances, T was diphasic in one lead.

Occasional variability in the height of the T wave was seen in the same record in association with the respiratory curve.

Two of ten children, in whom electrocardiograms were taken daily for five days in succession, showed marked variability of the T wave from day to day. In one child, the T wave in lead III, which showed an upwardly directed wave on the first day, revealed in the subsequent four days a progressive increase in the downward direction of the T wave closely simulating the effects produced by digitalis on the electrocardiogram of the same child. It can be distinguished as a normal change, however, by the fact that the S-T segment comes off directly from the descending limb of the QRS complex and does not fall below the iso-electric line (fig. 1). In one child whose T wave was negative in lead III to start with, it became positive on the fourth day and returned to negative spontaneously.

12. Weiss and Schwartz (footnote 9). Lincoln and Nicolson (footnote 11).

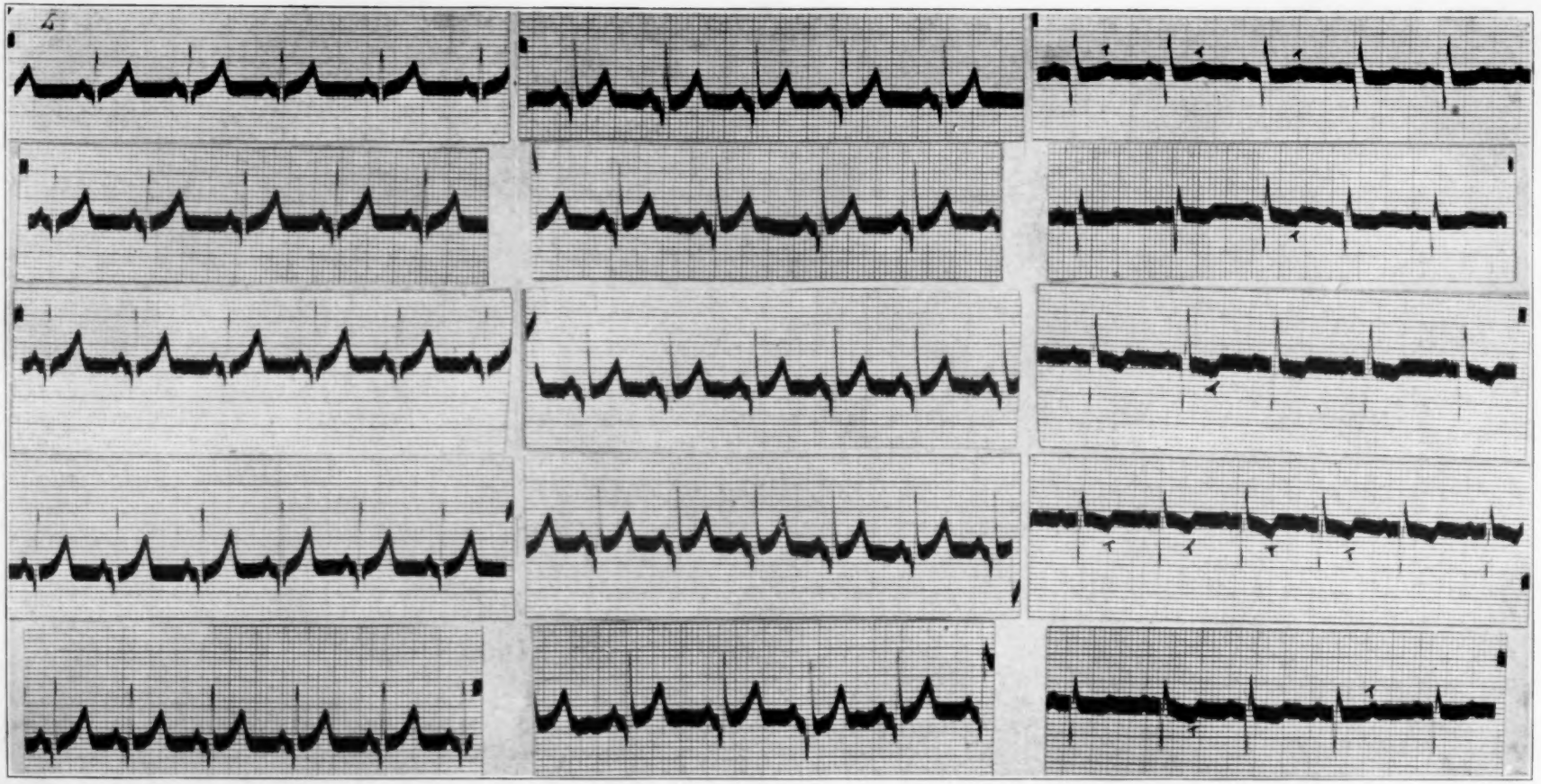

Fig 1.—Spontaneous variations in the T wave in lead III. Control records taken for five consecutive days in a child, aged 13, with chronic rheumatic valvular heart disease, who did not receive digitalis.

An appreciation of these spontaneous variations in the T wave of these children cannot be overestimated if one is to place any importance on the effects produced by digitalis on this particular portion of the electrocardiogram.

RESULTS OBTAINED WITH A SINGLE BODY-WEIGHT DOSE OF DIGITALIS IN CHILDREN WITH SINUS RHYTHM

Effect on the Symptoms.—The administration of a body-weight dose of digitalis in children with rheumatic heart disease with sinus rhythm during both the active and the inactive stage of the disease was not accompanied by any minor toxic manifestations such as nausea and vomiting. The children showed no objections to taking the drug provided it was well diluted with water. It cannot be said with certainty, however, that any improvement in symptoms was noted following the use of this single dose. A slight but measurable diuresis observed in two children who showed edema of the lower extremities could not be definitely attributed to the use of the drug.

Effect on the Sinus Rate.—In view of the fact that the heart rate is reduced spontaneously during the sleeping hours, as has been shown by Boas [13] in his recent studies with the cardiotachometer, we have considered the changes induced by digitalis on the sinus rate as seen only during the waking hours. No matter what the sinus rate was before the administration of a body-weight dose of digitalis, within twelve hours after the use of the drug we have noted a definite slowing of the rate varying between 10 and 15 beats per minute. This was a transitory phenomenon, however, and did not last in any one child more than four days at the most. In some children this slowing was accompanied by a slight sinus arrythmia which was not present before the administration of digitalis. In five of eighteen children a noticeable slowing of the heart rate was observed two weeks after the beginning of the experiment, but this could not be definitely attributed to the use of the single dose of the drug. As a rule, the maximum changes in the T wave were noted to be present at a time when the sinus rate was slightly higher than normally. As the T wave changes assumed their normal contour, the sinus rate became relatively normal, that is, the heart rate was observed to be the same at the end of the experiment as it was at the beginning.

Effect on the S-T and T Segments.—Eleven of the eighteen children with sinus rhythm showed signs of activity at the time of the first experiment was carried out, while seven were in the inactive state of rheumatic fever. In the former group there were four children in whom the administration of digitalis produced no effects on the electrocardiogram, while in the latter there were two. In other words, in one third

13. Boas, E. P.: The Cardio-Tachometer, Bull. New York Acad. Med. **4**:445, 1928.

of the children no effects were observed in the electrocardiogram after the use of a body-weight dose of digitalis. A single child with marked sinus bradycardia and a noticeable sinus arrhythmia in whom the ventricular rate averaged 50 beats per minute showed no changes in either rhythm or rate following the administration of digitalis. Two of three children in whom no variations were observed following the administration of the first body-weight dose of digitalis were found responsive to a similar dose of the drug several months later. Whereas at first there were no noticeable changes in their electrocardiograms, in the subsequent experiments the electrocardiograms showed all of the changes usually observed.

In the twelve children in whom positive changes were obtained following the use of a body-weight dose of the drug, the alterations noted in the electrocardiograms from day to day did not differ materially from those reported in normal adults,[1] with the exception, however, that the variations in the S-T segments and the T waves, although definitely established, were inconstant and not uniform in their progressive appearance. They were variable from child to child.

The most common change noted was a diminution in the size of the T wave from day to day with final inversion of the upright T waves sometimes only in one lead but more commonly in leads II and III. As the T wave diminished in size and came nearer to the iso-electric line, the S-T segment became markedly delineated. With this change there was a progressive lowering of the S-T interval below the iso-electric line which was especially noticeable in twelve of our children before the T wave finally became negative. The appearance of a maximum negativity of the T wave varied from child to child, the earliest being well defined on the fourth day, whereas the latest occurred on the fourteenth day after the administration of the drug (figs. 2, 3 and 4).

The reduction in the size of the T wave and its final negativity seemed to bear no relationship to the original size of the T wave. For example, a positive T wave in lead I which was 5 mm. in height became negative on the fourth day in one child, whereas a similar wave only 2 mm. high did not show any signs of negativity in another child until the ninth day.

In two children who showed a negative T 3 wave before the use of digitalis, the wave became postitive after its administration.

The Duration of Changes Induced by Digitalis on the Electrocardiogram of Children with Sinus Rhythm.—The changes in the S-T segments and the T waves of the electrocardiogram of children with sinus rhythm and heart disease varied in their duration after the administration of a body-weight dose of digitalis. If the return of the original electrocardiograms may be taken as criteria, these changes may last

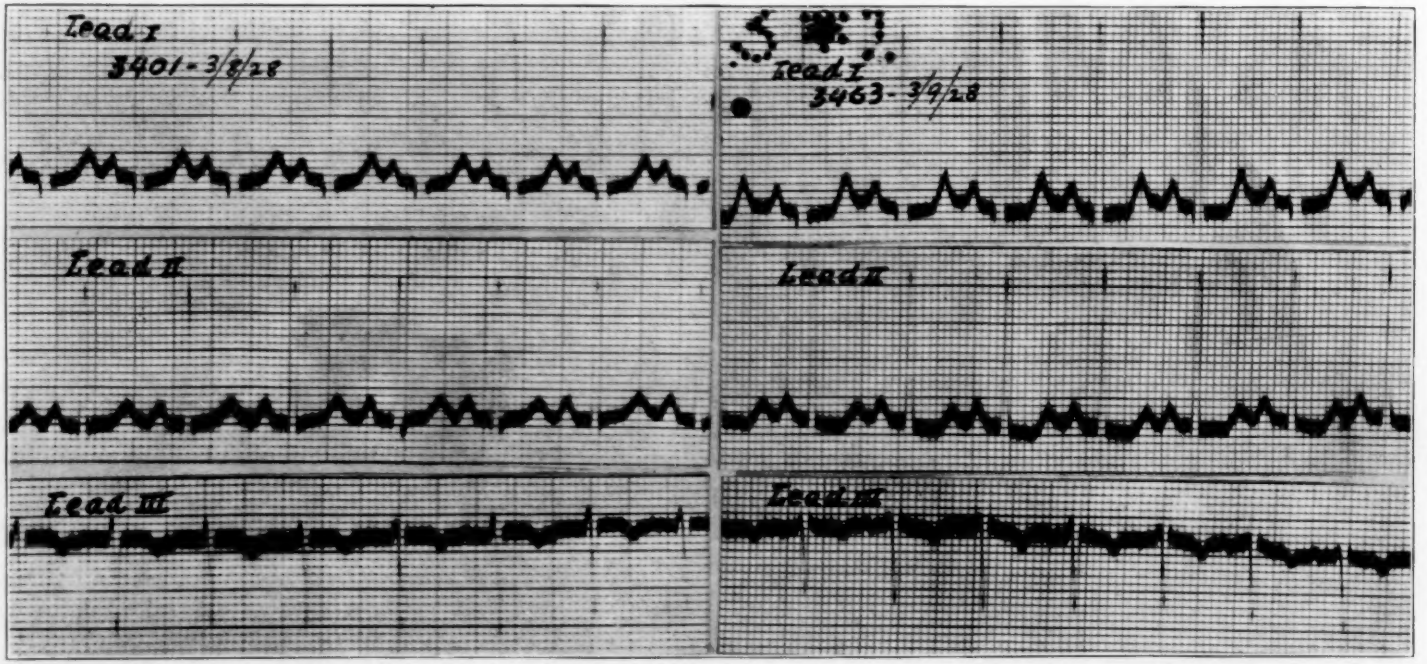

Fig. 2.—Comparison records before and after the administration of digitalis in a girl, aged 9½ years. The first change induced by digitalis is a lowering of the S-T segment below the iso-electric line, best seen in lead II.

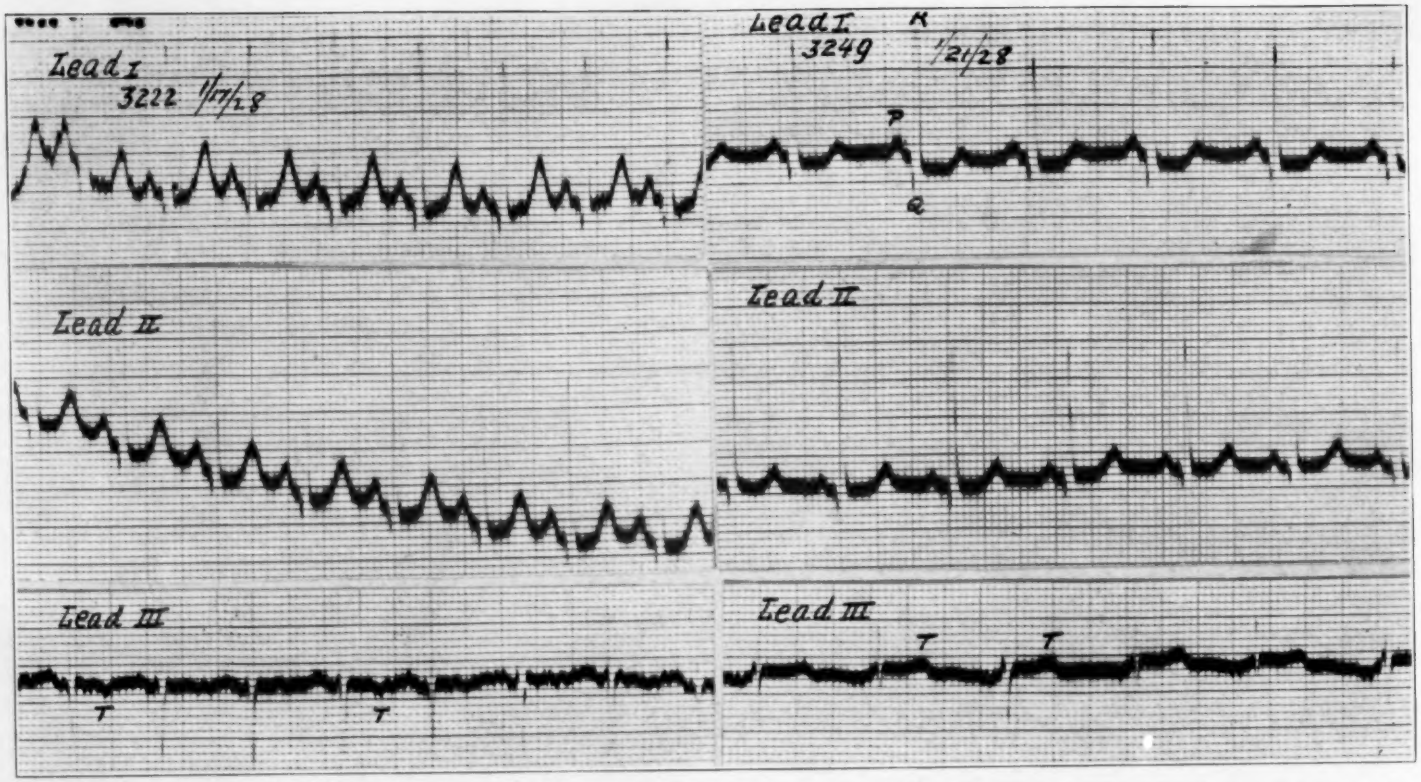

Fig. 3.—Comparison records before and after the administration of digitalis in a girl, aged 9 years. The second change induced by digitalis is a diminution of the T wave and a slowing of the sinus rate which is transitory. In lead III a downwardly directed T wave may be seen to become positive after the administration of digitalis.

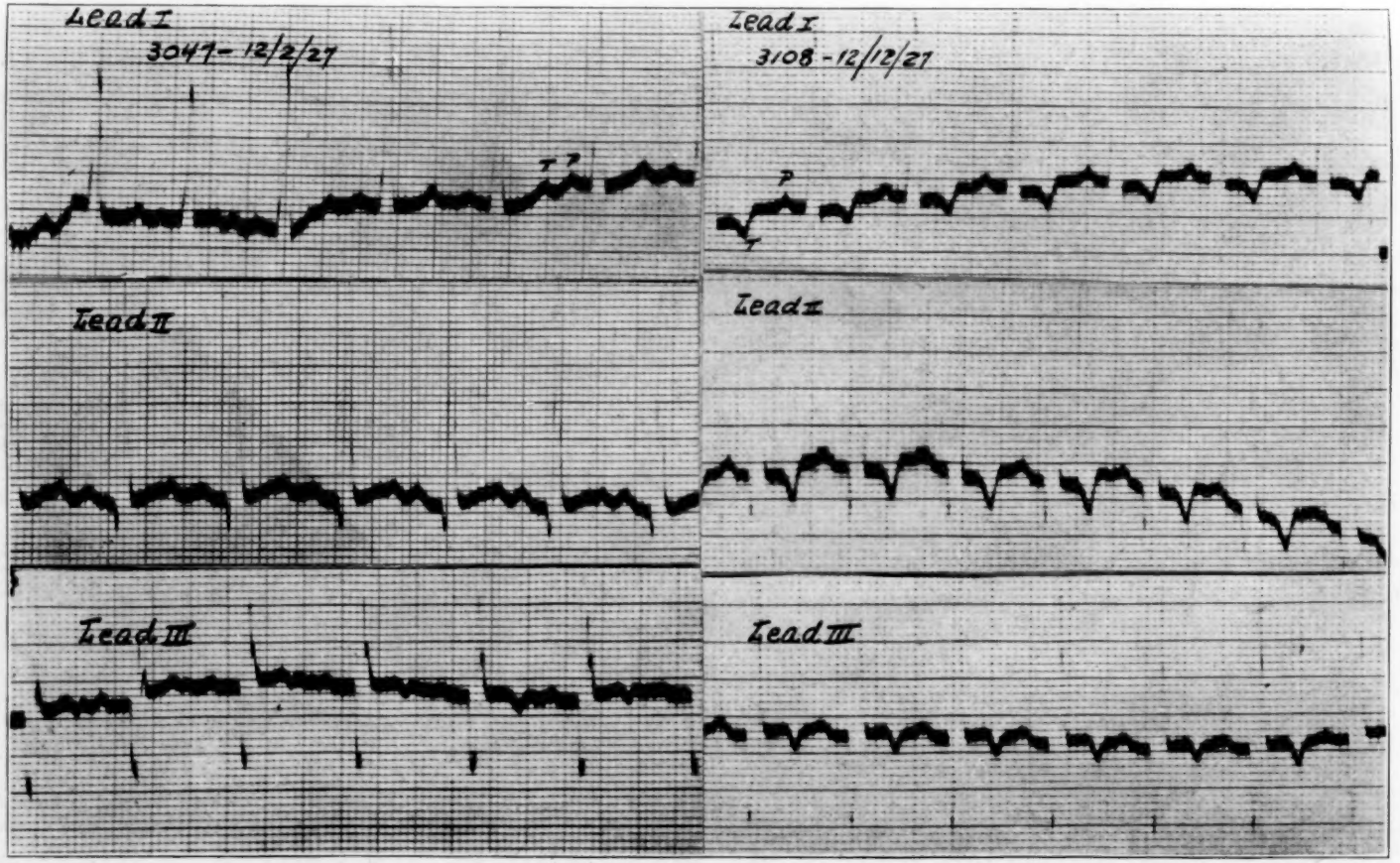

Fig. 4.—Comparison records before and after the administration of digitalis in a boy, aged 15 years. The maximum changes induced by digitalis may appear as late as ten days after the administration of the drug. Note the marked negativity of the T wave in all three leads.

from seven to as long as thirty-seven days. There is no relationship between the persistence of the changes in the S-T segments or the T waves of the electrocardiogram and age, weight or activity of rheumatic fever of the child. The return of these waves to normal is as variable as their appearance. In several instances, however, it was noted that T3 was the last wave to become normal.

Results Obtained with a Body-Weight Dose of Digitalis in Children with Sinus Rhythm

No.	Sex	Age	Weight, Pounds	Dose of Drug, Cc.	Valve Lesion*	Signs of Decompensation	Signs of Activity	Results Obtained	Duration of Action of Drug in Days†
1	F	4½	38	5.70	M.S., M.I.	Enlarged liver	..	No effects	
2	M	5	41	6.15	M.S., M.I.	Enlarged liver	..	T_1 reduced in size; T_2 diphasic; T_3 progressively negative	19
3	M	6½	40	6.00	M.S., M.I., A.I.	Enlarged liver	+	No effects	
4	F	7½	49	7.35	M.S., M.I.	Enlarged liver; edema; ascites	+	$-T_1$; T_3 reduced in size	16
5	F	8	44	6.60	M.S., M.I.	Enlarged liver; edema; ascites	+	T_1 reduced in size; $-T_2$ on fourth day; T_3 became positive and remained so	37
6	M	8	69	10.40	M.S., M.I.	Enlarged liver	+	$-T_1$; $-T_2$; $-T_3$	24
7	F	9	56	8.40	M.S., M.I., A.I.	Enlarged liver	+	No effects	
8	M	9	50	7.50	M.S., M.I., A.I.	Enlarged liver	+	No effects	
9	F	9½	47	7.00	M.S., M.I., A.S., A.I.	Enlarged liver	+	T_2 diphasic	22
10	F	10	78	11.70	M.S., M.I.	Enlarged liver	..	S-T lowered in 12 hours; —T reduced in size	17
11	F	10	69	10.40	M.S., M.I.	Enlarged liver	+	T_1 reduced in size; $-T_2$; $-T_3$	20
12	M	10½	58	8.70	M.S., M.I., A.I.	Enlarged liver	+	$-T_1$; T_2 reduced in size	8
13	M	11½	56	8.50	M.S., M.I., A.I.	Enlarged liver	+	No effects	‡
14	M	11	72	10.80	A.I.	.....	..	No effects	
15	F	12	76½	11.50	M.S., M.I., A.I.	.....	..	$-T_1$; $-T_2$; $-T_3$	18
16	F	12	63	9.50	M.I.	.....	..	$-T_2$; $-T_3$	7
17	M	14	96	14.40	M.S.	Enlarged liver	..	No effect	
18	M	13	110	16.50	M.S., M.I., A.S., A.I.	.....	..	$-T_3$	30
19	M	15	110	16.50	M.S., M.I., A.S., A.I.	Enlarged liver; edema of legs	+	$-T_1$; $-T_2$; $-T_3$	14

* In this column, M.S. equals mitral stenosis; M.I., mitral insufficiency; A.S., aortic stenosis, and A.I., aortic insufficiency.

† As judged by the persistence of the changes induced by digitalis on the S-T interval, and T waves of the electrocardiograms and their return to normal.

‡ Child with sinus bradycardia.

Effect on the P-R Interval.—In one child who was in the inactive stage of rheumatic fever before the experiment, an attack of rheumatic fever was ushered in shortly after the administration of the drug. The records of this child revealed a progressive increase in the P-R interval from the day that fever set in (fig. 5). Since such changes were not noticed in any other child with sinus rhythm it is fair to assume that

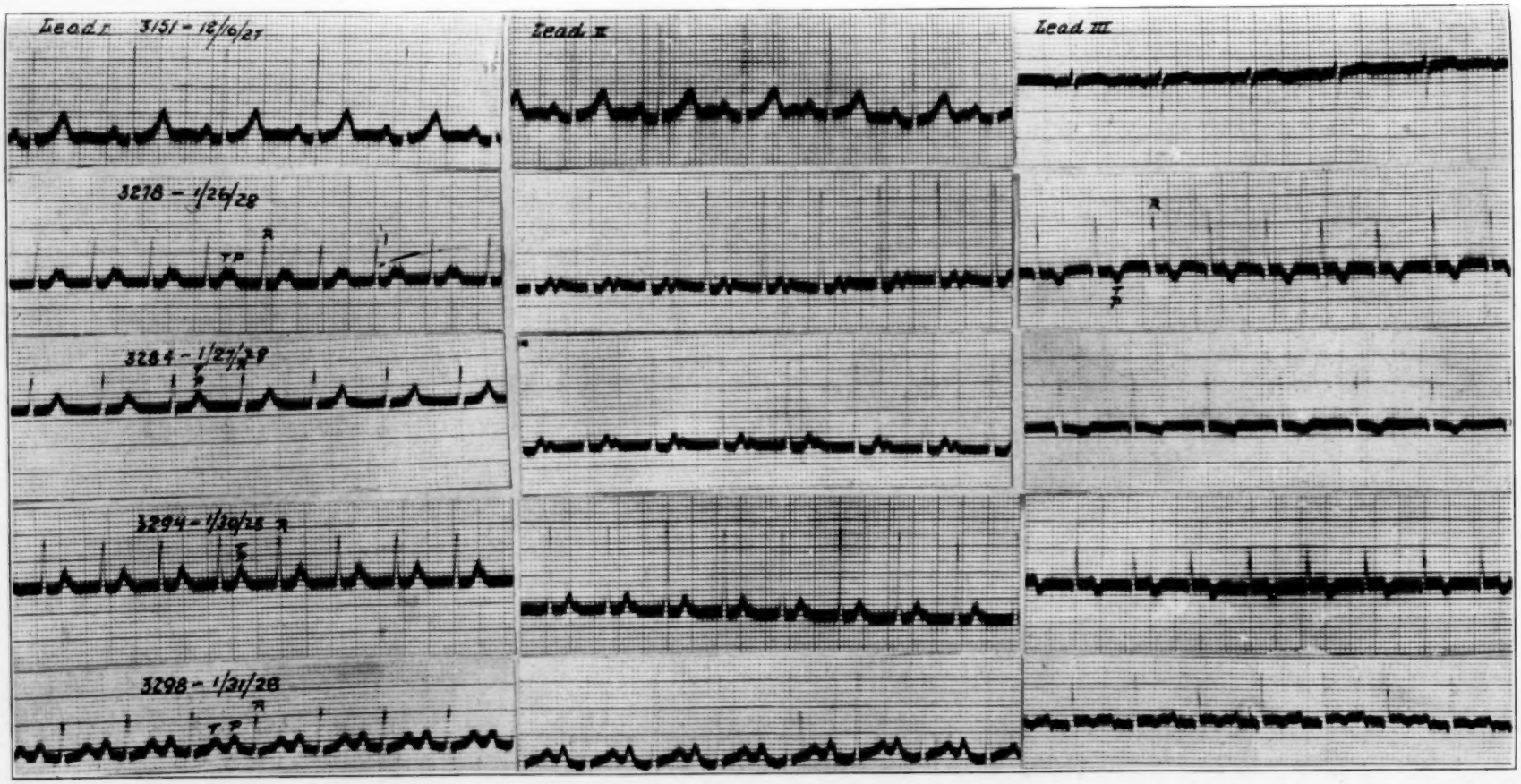

Fig. 5.—Progressive increase in the P-R interval coming on during an attack of rheumatic fever following the administration of a body-weight dose of digitalis in a girl, aged 10 years. Note that the rate is increased at the same time that conduction is prolonged, despite the conduction defect.

the administration of the body-weight dose of digitalis augmented the increase in the P-R interval. The belief that this change is in part due to digitalis and not solely to rheumatic fever may be gained from the presence of concomitant changes noticed in the S-T segment and the T waves of the electrocardiograms of this child. The T wave did not resume its original shape and size, however, until the twentieth day after the administration of the drug. The P-R interval returned to normal suddenly while the changes in the T wave were slow in their regression. In the other children with sinus rhythm the P-R interval was practically the same after the use of the drug as before its administration.

RESULTS OBTAINED WITH A SINGLE BODY-WEIGHT DOSE OF DIGITALIS IN CHILDREN WITH AURICULAR FIBRILLATION

Effect on the Symptoms.—The most distressing symptom in children with auricular fibrillation of the chronic or permanent form is extreme breathlessness.[14] The relief of dyspnea that follows the administration of a single body-weight dose of digitalis in such children is as spectacular as it is in adults with a similar cardiac irregularity, provided the children are responsive to the drug. The relief of dyspnea is proportional to the slowing of the ventricular rate. In five children with this arrhythmia in whom the drug was given at the height of an active attack of rheumatic fever at a time when the ventricular rate was a high as 150 beats per minute there was neither slowing of the ventricular rate nor relief of the shortness of breath. In the same children, the respirations became almost normal within twenty-four hours after the administration of a single body-weight dose of digitalis at another time when they did not show evidences of active rheumatic fever. In one child the respirations were eased only following a thoracocentesis after the ventricular rate had been slowed on the preceding day.

Effect on the Ventricular Rate.—In this series of children with chronic auricular fibrillation in whom it was possible to repeat the experiment on several occasions, a slowing of the ventricular rate following the administration of a single body-weight dose of digitalis was obtained only at a time when the children were in the inactive stage of rheumatic fever. During such a time an appreciable slowing of the ventricular rate was observed as early as two and one-half hours after the administration of a single body-weight dose of digitalis. In two children in whom electrocardiograms were taken every fifteen minutes for twelve hours, the ventricular rate was reduced progressively from an average of 157 beats a minute to 100 within twelve hours after the

14. Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children: Its Relation to Rheumatic Heart Disease, Am. J. Dis. Child. **36**:22 (July) 1928.

drug was given; on the following morning, twelve hours later, the ventricular rate was approximately 60 beats a minute. In these two children, the slowing of the ventricular rate preceded the changes in the T wave.

In two children it was noted that during an active attack of rheumatic fever while the ventricular rate was not affected by the drug, the T waves showed changes which were totally inconstant in their appearance and not measurable.

Effect on the S-T and T Segments.—In children with auricular fibrillation it is difficult to measure appreciable alterations in the S-T segments and the T waves of the electrocardiogram following the use of digitalis because the fibrillatory waves of the auricles are frequently superimposed on these segments and the T waves vary from beat to beat. Nevertheless, in the children with active carditis in whom the ventricular rate remained uninfluenced by the drug, the T waves showed definite progressive diminution in the size and negativity from day to day, but these changes were inconstant in their appearance. In the two children in whom digitalis slowed the rate, as seen from the electrocardiograms taken at frequent intervals throughout the day, the changes in the T wave were noted to follow the slowing of the ventricular rate. The maximum changes appeared on an average of three days after the maximum slowing had taken place.

SUMMARY

A summary of the results obtained from the administration of a single body-weight dose of digitalis to twenty-four children with chronic rheumatic valvular heart disease and signs of heart failure reveals that the use of the drug by this method is a safe precedure in children exhibiting sinus rhythm or an irregular ventricular rate due to auricular fibrillation. There were no untoward symptoms from the administration of the drug in a single dose of this type provided it was well diluted with water.

The changes induced by the drug were recorded in twelve of eighteen children with sinus rhythm and in five children with auricular fibrillation who were studied during both the active and the inactive phases of rheumatic fever. Moreover, in six of the eighteen children no electrocardiographic signs of digitalis action were observed.

The alterations produced by digitalis on the electrocardiograms of these children consist essentially of a lowering of the S-T segment below the iso-electric line with final progressive increases in the negativity of the T wave in one or more of the leads in which it was previously upright. In two children, a previously negative T wave in lead III eventually became positive.

These changes varied in their appearance from child to child and in the same child from time to time when the experiments were repeated.

The alterations produced by digitalis on the electrocardiograms of children with rheumatic valvular heart disease and signs of heart failure are also variable. They may last from a minimum of seven days to a maximum of thirty-seven days.

A body-weight dose of digitalis produced a transitory slowing of the sinus rate of between 10 and 15 beats per minute in twelve children with sinus rhythm. The same dose administered to children with auricular fibrillation at a time when there were no evidences of active carditis and when they were responsive to the drug reduced a ventricular rate from an average of 157 beats per minute to 60 beats within twenty-four hours. In the latter group, there was a definite relationship between the slowing of the ventricular rate and the relief of the dyspnea.

In one child, the administration of a body-weight dose of digitalis augmented the size of the P-R interval during an attack of rheumatic fever.

The inconstancy and variability of the appearance and duration of the changes induced by body-weight doses of digitalis on the S-T interval and T waves of the electrocardiograms of children with rheumatic valvular heart disease and signs of heart failure make this method of studying the dosage of digitalis in children totally inadequate. For similiar reasons the effects of digitalis on the electrocardiograms of children cannot be taken as criteria in measuring the standardization of the drug, its rate of absorption and elimination or the daily amount necessary to maintain its persistent effects, known as the maintenance dose.

THE FREQUENCY OF ATROPHY OF THE SUBCUTANEOUS FAT FOLLOWING THE INJECTION OF INSULIN *

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During a routine physical examination of a diabetic child, an obvious loss of subcutaneous tissue from the upper and middle portions of both arms was noted (fig. 1). This loss of tissue occurred at the site at which insulin had been injected. A photograph of this child taken a year previously showed that some atrophy, while not marked, had nevertheless been present at that time. A search of the literature revealed that a number of authors had recently described the same condition. Depisch [1] and Barborka [2] were the earliest to note the disappearance of fat from the subcutaneous tissue in diabetic patients as the result of the injection of insulin. Both of Barborka's cases occurred in women, while of Depisch's five cases, four occurred in women and one in a man. Shortly thereafter, Davison [3] and Mentzer and Du Bray [4] each reported a case in a woman. The latter authors included in their report an examination of tissue removed from the site of the atrophy. It showed a loss of fat with fibrosis but no lymphocytic foci indicative of inflammation, in contrast to the inflammatory tissue found in narcotized persons, the result of unclean hypodermic needles and syringes. Carmichael and Graham [5] reported three cases, two in women and one in a boy, aged 8; Chapman,[6] in a letter, reported one case. More recently, Rabinowitch [7] noted the occurrence of atrophy of subcutaneous fat in eight of his patients, and Lawrence [8] in one. Priesel and

* Submitted for publication, May 7, 1929.

* From the Department of Pediatrics, Mount Sinai Hospital.

1. Depisch, F.: Ueber lokale Lipodystrophie bei lange Zeit mit Insulin behandelten Fällen von Diabetes, K'in. Wchnschr. **53**:1965 (Oct. 15) 1926.

2. Barborka, C. J.: Fatty Atrophy from Injections of Insulin, J. A. M. A. **87**:1646 (Nov. 13) 1926.

3. Davison, R. A.: Absorption of Subcutaneous Fat Deposits at Site of Repeated Insulin Injections, California & West. Med. **26**:210 (Feb.) 1927.

4. Mentzer, S. H., and Du Bray, E. S.: Fatty Atrophy from Injections of Insulin, California & West. Med. **26**:212 (Feb.) 1927.

5. Carmichael, E. A., and Graham, G.: Local Fat Atrophy Following Insulin Injections, Lancet **214**:601 (March 24) 1928.

6. Chapman, P. D. H.: A Letter, Lancet **214**:674 (March 31) 1928.

7. Rabinowitch, I. M.: Atrophy of Subcutaneous Fat Following Insulin Injections, Canad. M. A. J. **18**:560 (May) 1928.

8. Lawrence, R. D.: The Effect of the Prolonged Use of Insulin on the Subcutaneous Tissues, Lancet **214**:1328 (June 30) 1928.

Wagner[9] described two cases of rather severe local lipodystrophy following the injection of insulin in diabetic children and noted that mild degrees of this condition occur frequently.

OBSERVATIONS

I can substantiate their statement and desire to record that the loss of subcutaneous tissue occurs far more frequently than has previously been noted. On careful examination of twenty-four diabetic children in the clinic who were receiving insulin, I noted a slight loss of subcutaneous fat about the site of the injections in eight children; a moderately severe loss in four, and a severe loss at one or more sites in four (figs. 2 and 3). In eight children there was no evident loss of subcutaneous fat. In addition, if one palpates the site of injec-

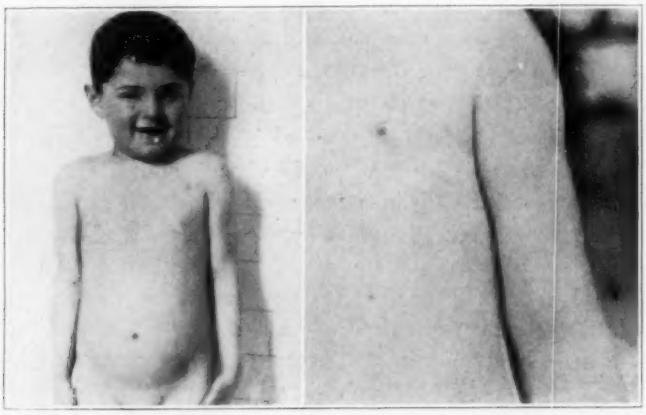

Fig. 1.—*A*, marked atrophy of the subcutaneous fat of both arms; *B*, closer view of same patient.

tion of insulin within an hour after the time of injection, one usually notices a local warmth. One child, who had been receiving insulin for only six months, showed beginning disappearance of subcutaneous fat in spite of the fact that the child's parent injected insulin alternately in all four extremities. The mild atrophy which is present in some patients would not have been noted had not the more severe forms called attention to the possibility of the disappearance of fat in all patients who have been receiving insulin for any length of time. At first one can feel a slight flatness of the tissue in the upper part of the arm or in the thigh, the usual sites of injection, which progresses until a definite depression is noted. If the injections are

9. Priesel, R., and Wagner, R.: Ueber lokale Lipodystrophie nach Insulininjektionen, Ztschr. f. Kinderh. **46**:453, 1928.

continued at that site, the process increases until there is only muscle, bone and indurated skin about the site of the needle punctures. The size of the atrophy usually varies from 2 to 10 cm. in width. Only two of fifteen children failed to show atrophy after more than one year of treatment with insulin. A number of adult diabetic patients were carefully examined to determine if this phenomenon was as common

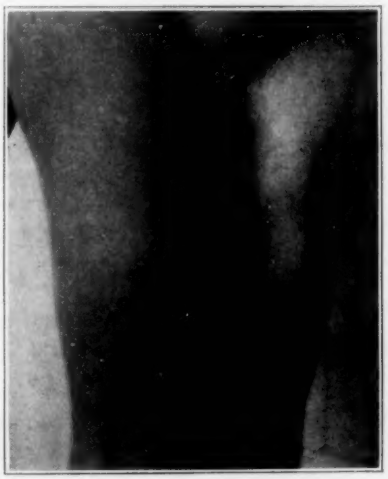

Fig. 2.—Moderately severe atrophy of the fat of both thighs.

Fig. 3.—*A*, atrophy of the fat of both buttocks; *B*, atrophy of the fat of the upper arm of the same patient.

in them as in children. A fair proportion of these patients showed some loss of subcutaneous fat.

All observers agree that the fat disappears only about the sites of the injections of insulin and that no general lipodystrophy is present. The fat disappears not only at the site of the needle puncture, but also somewhat above this point in the arm and usually below in the

thigh, depending on the direction in which the needle is pointed and the path along which the insulin travels. In children who inject insulin into themselves, the atrophy seems in some instances to be more marked, probably because these patients become accustomed to reinject the insulin into the same site, despite repeated warnings.

Few, if any, of the patients with atrophy have at any time complained of pain following the injections of insulin. They have not noted the disappearance of fat from the tissues, although in several instances the parents have noted that they have had to shift the site of injection because of thinness of the subcutaneous tissues. The intensity of the diabetes has not been altered in the children who show lipodystrophy.

Shortly after the discovery of insulin, local tissue reactions with necrosis and abscess were common, but since the purification of insulin by the removal of protein, that type of reaction occurs rarely. None of the cases here reported come in that category, and except for the mentioned warmth of the tissues for a short time following the injection of insulin, which is readily apparent to the touch, there is no evidence of any inflammatory reaction. It does not seem probable that the small amount of protein which may remain after purification is the cause of the lipodystrophy. The number of units injected is not a factor. Several cases have occurred following the injection of as small a maximum dose as 6 units twice daily. Squibb's, Stearns' and Lilly's insulin have all been used by the patients. No single product has been used by any one patient continually. The state of tissue nutrition is apparently not a predisposing factor, since loss of fat has occurred in well nourished as well as in thin diabetic children.

There has as yet been no satisfactory explanation for the occurrence of local lipodystrophy. There are two main possibilities: (1) that the disappearance of the fat is due to the preservative added to the insulin, and (2) that it is due to the insulin itself. Priesel and Wagner expressed the belief that the lipodystrophy is caused by tricresol, which is added in small amounts (0.1 per cent) to insulin for antiseptic purposes. They thought that it causes a tissue damage and prevents the building of fat at the site of injection. According to their theory, while the nutrition of the subcutaneous tissues and the building of fat go on in other parts of the body, these cannot occur at the points of injection because of the tricresol. Against this view is the fact that lipodystrophy occurs in portions of the body well supplied with fat, such as the buttocks, even in malnourished children. It seems more likely that the injected material destroys the fat that is present, yet it may at the same time prevent the formation of new fat at the site of injection. Moreover, most manufacturers have now replaced tricresol by a small amount of phenol, which, as far as is known, has no

lipolytic action. It must be said, however, that no drug which contains even a small amount of preservative has ever been injected as frequently as insulin. Vaccines and other biologic products that contain a preservative have never been known to cause a disappearance of subcutaneous fat, but these have not been injected frequently enough to show that the loss of fat could be caused by the preservative. Rabinowitch has shown that the cause does not lie in the needles or the syringes or in the compound solution of cresol in which needles have been kept. Atrophy occurred in some patients who boiled their needles and who did not use compound solution of cresol or other disinfectants.

Carmichael and Graham suggested that the cause is the presence of a small amount of lipase in insulin. The laboratories of three American firms state that their product contains no lipase; Rabinowitch concentrated large amounts of insulin at a low temperature and reduced pressure and then tested the material for lipase and found it absent. Lawrence's experiments likewise show the absence of lipolytic ferment in insulin. He injected small amounts of insulin into one of the muscles of the thigh for three years, then did not use that site for two years and at the end of that time excised some tissue which showed fibrosis with loss of muscle fibers. His results are open to the possible criticism that the insulin which was used in the early part of his work may not have been protein-free. Bowie and Robinson [10] also showed that insulin causes necrosis when injected into muscle, but the insulin which they used was also manufactured shortly after its discovery. In this connection the recent report of Light and Torrance [11] is of interest. These authors show that morphine addicts, probably because of uncleanliness in handling their syringes, frequently produce numerous superficial abscesses in the subcutaneous tissues. Acute inflammation with abscess has not been present at any time in the cases included in this report. At rare intervals, several of my patients have had superficial abscesses which were due to infection.

It has been suggested that a local vasomotor disturbance produces the atrophy. The galvanic and faradic response of muscles about the site of insulin atrophy, however, has been normal in several patients who have been examined. Avery [12] believed that the injection of insulin or other substances damages the delicate protoplasmic cell envelop of

10. Bowie, D. J., and Robinson, W. L.: Histological Study of Muscle Degeneration Produced by Local Injections of Insulin, J. Lab. & Clin. Med. **8**:569, 1923.

11. Light, A. B., and Torrance, E. G.: Opium Addiction: Physical Characteristics and Physical Fitness of Addicts during Administration of Morphine, Arch. Int. Med. **43**:326 (March) 1929.

12. Avery, H.: Insulin Fat Atrophy: A Traumatic Atrophic Panniculitis, Brit. M. J. **1**:597 (March 30) 1929.

the fat cells so that fat globules are released and that they, acting as foreign bodies, result in the formation of histiocytes which take on lipophagic activity. The most plausible explanation seems to be that a low-grade inflammatory process is set up by the repeated injections of insulin and that the resultant damage causes a disappearance of the soft areolar tissue owing to replacement by scar tissue. Local warmth, which one frequently feels, is in line with this idea. It must be said, however, that subcutaneous injections of other drugs do not cause the disappearance of fat, although few drugs are injected as frequently as insulin. It is also possible that insulin raises the local tissue metabolism, which, when cumulative, results in the disappearance of fat by oxidation. There is, however, no evidence to prove this contention.

CONCLUSIONS

1. Careful examination of twenty-four diabetic children who had been receiving insulin for more than six months revealed that sixteen had a local lipodystrophy about the site of the injections of insulin.

2. The frequency with which this phenomenon occurs has not been previously reported.

3. The cause of the disappearance of the fat is not apparent from the evidence at hand. It is most likely due to a low-grade inflammatory process.

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DIETARY CONTROL OF DENTAL CARIES*

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In a previous article, we reported the arrest of caries in the teeth of diabetic children who for periods of two months or longer had received carefully controlled diets designed to conserve the sugar-handling mechanism.[1] Repeated subsequent examinations of the teeth of these and of other diabetic children have confirmed these observations. No progression of caries has been demonstrable in any of the patients under this regimen. This has been interpreted as a response of the structure of the teeth to a diet furnishing essential vitamins and minerals in adequate amounts, and as indicating that in any healthy person such dietary adequacy should lead to the arrest of caries.

These diabetic diets differed from the diet usually considered as optimum for the normal child in that 70 per cent of the calories were supplied by fat. Moreover, the regimen of these children also differed from that of normal children, in that insulin was employed in practically every case.

The question was raised as to whether the arrest of caries was to be explained by some of these departures from the regimen of the normal child rather than by the adequacy of the diet. In order to answer this, further dietary observations have been made on nondiabetic children. The results form a basis for this report.

EXPERIMENTAL STUDIES

A group of nondiabetic patients in the children's orthopedic ward was chosen. At the initial observation, each child in the group had extensive caries, the activity being obviously demonstrable by the softness of the exposed dentine. The diets of these children were then made similar to those given to the diabetic children, the actual amounts in each case being determined by the height of the child. No insulin

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* From the Departments of Pediatrics and Dentistry, State University of Iowa.

* Read before the American Pediatric Society, St. Louis, May 20, 1929.

1. Boyd, J. D., and Drain, C. L.: The Arrest of Dental Caries in Childhood, J. A. M. A. **90**:1867 (June 9) 1928.

was given. Each meal was carefully supervised to insure that the prescribed diet was completely consumed. Four patients were kept on this regimen for two months or longer. In every instance the caries became arrested, the arrest being evidenced by the change in the consistency of the dentine from the initial state to one of stony hardness, with no advance in the destructive process.

It was possible to follow the subsequent course of two of these children. They returned to the ward routine at the close of the period of observation and remained in the hospital for several months. During that time they were offered the regular ward diet. The actual consumption of the food offered was not stressed, and as a result, they chose from each meal the foods that pleased them most and refused the remainder. Although the ward menus are designed to meet a child's needs fully, it is apparent that without careful supervision, the nature of the food intake may be persistently defective. After several months, both children were found to have active caries, and one had three new cavities.

The next study was made to determine whether arrest of caries could be obtained in the home, under a regimen which approximates that of the normal child. A group of children of preschool age was chosen, each of whom had actively progressive caries. In a conference with the parents, the purpose of the study was explained, and the cooperation of several was obtained. They were taught to select carefully the foods offered the children, so as to insure the intake of the recognized essential minerals and vitamins in considerable amounts, and to keep a record of the foods actually eaten each day. The sheet of instructions furnished them specified that each child should receive daily a quart of milk, one egg, a teaspoonful of cod liver oil, one ounce of butter, one orange, two or more servings of succulent vegetables and of fruits, and such other foods as the child desired. Candy was allowed after meals, but not at other times. No other noteworthy dietary restrictions were made, except that foods which were of a nonessential nature or which might displace from the diet some of the prescribed items were prohibited. Five children following the stipulated regimen were under observation until the caries had been arrested completely. In no instance did this require more than ten weeks. With the exception of one child who had developed otitis media, all gained weight during the period, three of them gaining at the rate of approximately half a pound each week.

The children in this group were receiving carbohydrate, protein and fat in liberal quantities. The diabetic and orthopedic groups received limited amounts of carbohydrate, but little free sugar, and large amounts of fat; their protein intake was about the same as that of the preschool group. These dietary differences are apparently of minor importance

in the arrest of caries. This is further indicated by observations of another group of children, whose calories were supplied chiefly as sugars and other simple carbohydrates, with about twice the amount of protein that the other children received and practically no fat. This group consisted of four girls with celiac disease, a condition in which the tendency to dental caries is notorious. In this condition, the ability to absorb fat and starch is impaired, necessitating the use of simple sugars and protein as sources of nutrition.

The two older children had extensive caries when they first came under treatment. The two younger ones, 25 and 31 months old, had not yet developed caries when first seen. The four have been under observation at irregular intervals for more than three years. During that time, they have been under the dietary management just described for the control of the celiac condition. The two younger children have not yet developed any caries, and that of the other two has become arrested in the same manner as in the other groups discussed.

In correlating the diets of these four groups of children, it is apparent that they differ widely yet seem equally effective in arresting caries. In one, calories were supplied principally as simple sugars, and fats were avoided as much as possible; in another, fats furnished most of the energy, and only enough carbohydrate was used to make the diets anti-ketogenic. In certain essential features, however, the diets were similar. Each child received cod liver oil, orange or tomato juice, milk, vegetables and fruits daily, in amounts designed to meet the requirements for vitamins and minerals. The protein allowance in every instance was at least a gram per pound of body weight. Whatever the factors essential for dental integrity, they apparently are supplied by these foodstuffs.

The question at once presents itself, Why is carious activity so prevalent in uncontrolled groups, and why is its arrest in childhood so infrequently observed, if simple foods are adequate as preventives and correctives? Our answer is that children's diets are seldom as adequate as they appear at first glance. Even when children's menus are carefully planned, the foods that the child eats may be considerably different from those prescribed. Unless supervised, the child's diet will be governed by his food preferences, and foods which are not liked will not be eaten. This was well illustrated by the orthopedic patients whose caries became active after strict supervision of feeding was discontinued. It was even more evident in three of the preschool group who were members of the same family. The mother assured us at the outset of the study that her children were receiving essentially the diet we were recommending, yet they had active caries. She admitted, however, that she was not sure how much of the foods she served were actually being eaten by the children. After keeping a careful record of their intake under the new regimen for two weeks and noting a substantial gain

in weight of each child during that period, she volunteered the information that her children were now eating all the foods on the menu, whereas previously they obviously were not.

These observations indicate that tooth decay is dependent primarily on metabolic changes. This is not in accord with the usual concept of caries. While the influence of diet on the production of caries is recognized, the effect of food is generally explained on the basis of the resultant acidity of the mouth and the erosion of the tooth by the acid products of bacterial action. With this as a premise, caries has been credited to diets high in sugar and starch, augmented by poor hygienic care of the mouth.

If the acidity of the mouth were a primary factor, we would expect to find evidence of lessened production of acid in the mouths of children with arrested caries. This has not been the case. Measurements of salivary acidity have shown no consistent difference in the reaction of the saliva of those with arrest as compared with those in whom the caries was actively progressing.[2] Furthermore, the potential ability of the oral flora to produce acid has been found to be as great in the group with arrested caries as in the group with active caries. Cultures of peridental scrapings, grown under conditions favorable for the production of acid, showed that the flora had as marked an acid-producing capacity after caries had been arrested as was found in the same children before dietary control was instituted.[3] In many instances, large cavities which necessarily would retain food débris were purposely left unfilled for several months in the mouths of children who were receiving general diets, including bread, potatoes and candy, but who were eating the foods specified as essential. In none of these did the caries progress.

The oral hygiene in the homes of many of these patients was not good. Some of the children with arrest of caries did not use a toothbrush while away from the hospital. Deposits of calculus occurred, which in some instances were extensive, but the lack of oral cleanliness did not seem in any way to deter the arrest of caries.

These observations have not pointed to any one food component as specific in the maintenance of dental integrity. Our present concept is that it may depend on the adequacy of the diet in all essential factors. Nothing has been noted which would indicate that the arrest of caries was primarily dependent on the limitation of the amount of any of the foods commonly used. However, the use of any component in excessive amounts may lead to the omission from the diet of other essential foods, and such omission may render the teeth susceptible to decay. If

2. Roskin, M.: Mineral Content of Saliva of Children with Arrested Caries, Proc. Soc. Exper. Biol. & Med. **25**:465, 1928.

3. Magee, C.; Drain, C. L., and Boyd, J. D.: Dental Caries; Influence of Potential Mouth Acidity, Proc. Soc. Exper. Biol. & Med. **126**:718, 1929.

extensive use of sugars and starches is found associated with caries, it is probably to be explained on this basis.

It is worthy of special note that it has not been necessary to use mineral mixtures, such as are being exploited as therapeutic dietary accessories, to supplement the mineral content of these diets. Apparently the essential minerals have been supplied in adequate amounts by the use of menus which were simple in nature and readily obtainable.

SUMMARY

Dental caries has been arrested in many instances, under divergent conditions of health and environment, by the ingestion of diets high in mineral and vitamin content. All diets were designed to give adequate protein and calories, but in other respects they varied widely in nature. The arrest usually became apparent after about two months of dietary control. On the basis of the clinical and experimental observations, it is thought that active caries should be viewed as indicative of nutritional deficiencies. These deficiencies may not make themselves obviously apparent in any other way. Yet when the food intake is made adequate, caries will become arrested, and in other respects there will be evidences of better health.

BLOOD CULTURES AFTER TONSILLECTOMY*

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I. M. EPSTEIN, M.D.

AND

MARIE WERNER, B.S.

CHICAGO

Doubt as to the entire harmlessness of tonsillectomy has been voiced frequently. The occasional occurrence of cases in which a new infection or the "lighting up" of an old one has followed suggestively close on the heels of tonsillectomy cannot be ignored. But there is almost no experimental proof of the relation between the two events.

A case in point is that of a girl recently admitted to the Children's Memorial Hospital. She had had a tonsillectomy done eleven days previously. The day following the operation she had an acute attack of severe abdominal pain, accompanied by fever and vomiting. Less severe pain persisted until the day of admission, when at operation a large appendical abscess was found. The facts are suggestive of a causal relation, but are certainly not conclusive.

We thought that some direct evidence bearing on similar occurrences might be obtained by investigating whether bacteremia sometimes follows tonsillectomy.

For this study, blood cultures were taken of seventy-eight patients selected from a large group of children admitted to the hospital for tonsillectomy. In order that we might have the presumably optimum conditions for finding bacteremia, we selected only those patients who gave a history of a recent infection of the throat or showed the evidence of one.[1] Injection of the pillars, tonsils and pharynx was considered evidence of recent infection. In some of the children the tonsils were large, in others small. In practically all they were cryptic or ragged. Definitely enlarged cervical lymph nodes were present in almost every case. Many showed a purulent postnasal discharge (table 1). In no case was the preoperative temperature above 99.8 F. rectally.

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* Submitted for publication, June 4, 1929.

* From the Otho S. A. Sprague Memorial Institute Laboratory and the Children's Memorial Hospital.

1. Ordinarily, children who have had a recent infection of the throat are not admitted for tonsillectomy, but of the 800 odd who were admitted for the operation during that time, we were able to find a number in whom the condition was suitable for our work.

From the histories we found that of the seventy-eight patients, thirteen had had acute sore throats within the two weeks preceding the operation. Nine gave a history of previous rheumatic infection of the joints, three of cardiac disease, four of nephritis, two of chorea and thirty-one of cervical adenitis (table 3).

PROCEDURE

Three blood cultures were taken in each case: the first immediately before operation; the second, within the half hour following the operation in thirty-three cases and either immediately after the removal of the first tonsil or immediately after the removal of the second tonsil in the remaining forty-five; the third from six to ten hours after the operation.

TABLE 1.—*Evidences of Throat Infection*

	Injected Pillars	Injected Pharynx	Injected Tonsils	Cervical Adenopathy	Postnasal Discharge	Ragged Tonsils	Cryptic Tonsils
Number of patients.....	68	44	48	71	20	25	42

TABLE 2.—*Rectal Temperatures at Time the Cultures Were Taken*

	99.8 or below	100-101	101-102	102-103	103-104
Second culture, number of patients.....	56	19	2	1	0
Third culture, number of patients.....	40	25	7	3	3

TABLE 3.—*Possible Complications of Throat Infections Given in Histories*

	Rheumatic Disease of the Joints	Cardiac Disease	Nephritis	Cervical Adenitis	Chorea
Number of patients.....	9	3	4	31	2

Cultures from the nose and throat were taken at the time of the first blood culture. The rectal temperature was taken at the same time that each blood culture was taken.

The tonsils were removed by dissection and snare or with the Beck instrument. The adenoids were removed with the LeForce adenatome. All the operations were done under ether anesthesia.

BACTERIOLOGIC TECHNIC

The blood was drawn from the veins of the cubital fossae. In fifty-seven of the cases, 8 cc. of the blood was inoculated directly into 50 cc. of warmed dextrose veal broth. In twenty-one of the cases the blood was defibrinated by shaking with glass beads, then immediately inoculated into different aerobic and anaerobic mediums. All mediums had a p_H of from 7.0 to 7.4. For strictly anaerobic mediums, dextrose brain broth was sealed with pyrogallic acid. All inoculated mediums were incubated for fourteen days before being discarded.

RESULTS

In none of the seventy-eight patients was a positive blood culture obtained.

Approximately half of the patients had a postoperative rise in temperature; in three of them the temperature rose above 103 F. (table 2). The fever was apparently not caused by a blood stream infection.

The predominating organisms found in the cultures from the nose and throat are shown in table 4.

COMMENT

Before beginning this work we thought it likely that there would be some positive cultures, because a tonsillectomy almost duplicates the conditions found most suitable for the production of bacteremia

TABLE 4.—*Predominating Organisms in Nose and Throat Cultures*

	Nose	Throat	Nose and Throat
Streptococcus viridans*	6	28	6
Streptococcus hemolyticus	3	4	2
Streptococcus anhemolyticus	..	..	8
Staphylococcus albus	18	6	10
Staphylococcus hemolyticus	3	..	..
Diphtheroids	4	..	..
Streptococcus viridans and Streptococcus hemolyticus	..	1	..

* No attempt was made to determine whether some of the green-producing cocci in chains were pneumococci.

in experimental work; that is, a fresh wound is made in a field teeming with bacteria, many of them pathogenic. Giami, referred to by Harter,[2] found such conditions ideal.

We realize that the failure to obtain positive blood cultures in these cases does not prove that there was no bacteremia. Blood returning from the tonsils must have passed through both the pulmonary and the peripheral capillary beds before reaching the cubital veins from which we took our cultures. This obviously allows a great dilution and may also have effected a sterilization of the blood from the field of operation. The fact has been repeatedly confirmed experimentally that moderately virulent bacteria injected into the blood stream soon disappear from the circulation. However, if there had been a bacteremia of considerable extent in any of our patients, we ought to have recovered some of the bacteria by our method.

2. Harter, J. H.: Significance of Bacteremia Following Mastoid Operations, Northwest Med. **24**:35 (Jan.) 1925.

That a bacteremia may occur and be demonstrated following surgical intervention in an infected field has been shown by Seifert,[3] who found nine cases of bacteremia following appendectomies in forty-three patients. Dabney [4] reported a case of bacteremia in a patient on whom a mastoid operation and a tonsillectomy were done at the same time. He assumed that as the blood culture showed anhemolytic streptococci while cultures from the mastoid and the middle ear had given repeatedly pure cultures of *Staphylococcus aureus,* the bacteremia resulted from the tonsillectomy.

We had considered drawing the blood for culture from the internal jugular veins, which directly drain the field of operation, but the possible risks involved in punctures of the internal jugular veins were considered too great to justify the procedure.

SUMMARY

1. Blood cultures were taken from seventy-eight selected patients following tonsillectomy.

2. All patients showed evidences of recent infections of the throat.

3. Positive blood cultures were not obtained in any case.

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3. Seifert, E.: Bacteremia After Operations, abstr., J. A. M. A. **85**:1924 (Dec.) 1925.

4. Dabney, V.: Bacteremia Due to Tonsillectomy Complicated by Mastoiditis, Arch. Otolaryng. **2**:362 (Oct.) 1925.

THE DETERMINATION OF THE VALUE OF SERUM IN THE TREATMENT FOR MENINGOCOCCUS MENINGITIS

REPORT OF AN ILLUSTRATIVE SERIES OF CASES *

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This is a report of a series of cases of epidemic meningococcus meningitis in the Babies' Wards of the New York Post-Graduate Hospital during 1928. It demonstrates some of the difficulties still to be faced in the successful serum treatment for this disease.

Cerebrospinal meningitis, first reported in Geneva, Switzerland, in 1805, by Viensseau and first reported in the United States in 1806,[1] has since been constantly present in the civilized world in endemic and in epidemic form.

Previous to the use of the serum treatment for the disease the mortality rate ranged between 25 and 90 per cent, depending on the severity of the infection. No treatment was of avail. Quincke opened up a new method of approach when he introduced the lumbar puncture as a therapeutic procedure in 1891. The intraspinous use of chemicals was attempted, but was not attended with success.[2]

During the epidemic of from 1904 to 1909, it was first proved that *Diplococcus intracellularis* of Weichselbaum is the sole cause of epidemic meningitis in man. During this period, the first effective serum was produced with which to combat this scourge.[3]

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* From the Department of Pediatrics and the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.

1. Ong, H. A.: The Serum Treatment of Epidemic Cerebrospinal Meningitis, Arch. Pediat. **30**:781, 1913.

2. Flexner, S., and Amoss, H. L.: Chemical Versus Serum Treatment of Epidemic Meningitis, J. Exper. Med. **23**:683 (March) 1916. Blum, L.: Treatment by Proteins and Specific Serum in Meningococcemia, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:83 (Jan. 19) 1923; abstr., J. A. M. A. **80**:1490 (May 19) 1923.

3. Flexner, S.: Antimeningitis Serum and the Results of Its Employment, Internat. Clin. **4**:1, 1909

Kolle, Wassermann and Jochman, in Europe, studying the effects on man, and Flexner,[4] in the United States, studying the effects on monkeys, announced encouraging results from the use of antimeningococcus serum in 1906.

The average mortality rate was reduced from 70 to 30 per cent by the use of Flexner's serum, with a shortened average duration of illness and lessened sequelae.[1]

Previous to the advent of the series of cases herein reported, the use of standard antimeningococcus serums in our wards had been attended by satisfactory results. Beginning with the first patient with meningococcus meningitis to enter the wards in 1928, however, we were chagrined to find that our hitherto effective treatment was valueless.

The present paper includes a report of the work done in search for a means of controlling this apparently resistant micro-organism.

Seven different standard and widely used serums were tried in an endeavor to find one which would be effective against the strains of meningococci which we were combating. In this presentation they are designated as: serums 1, 2, 2*a*, 3, 4, 5, 6 and 7. Serums 2 and 2*a* represent two lots of the same serum.

Before a curative serum could be found, ten deaths were recorded in the patients treated with five other serums. The use of the only effective serum we could obtain was followed by thirty recoveries in a series of thirty-four cases. In one of the fatal cases in this series the patient was admitted in a moribund condition on the fourth day of illness with a spinal fluid cell count of 53,200. The second was also admitted in a moribund condition after a severe but less acute course of twenty-two days' duration. The two remaining patients died of a complicating pneumonia after the serology of the spinal fluid showed marked improvement.

SYMPTOMATOLOGY

Meningococcus meningitis is protean in its manifestations, but certain signs and symptoms are of outstanding value in establishing the diagnosis. These are presented with the percentage of occurrence in this series of cases. Although they varied in degree of severity, if they were in evidence at all, they were included in these statistics.

The commonest symptoms were headache, fever and irritability, which were present in all patients old enough to signify their presence. The other symptoms are listed in order of frequency, with the percentage of occurrence in this series: Bulging fontanel, 100 per cent (in the four patients young enough); vomiting, 96.6 per cent; stiff

4. Flexner, S.: Experimental Cerebrospinal Meningitis and its Serum Treatment, J. A. M. A. **47**:560 (Aug. 25) 1906.

neck and Brudzinski's sign, each 93.3 per cent; marked general pain and malaise, 86.6 per cent; Kernig's sign, 76.6 (bilateral) plus 6.6 per cent (unilateral); opisthotonos, 80 per cent; irrationality or convulsive seizures, 6.6 per cent; changes in the tendon reflexes, hyperactive, 66; diminished or absent, 23 per cent; coma, 63.3 per cent; abnormal eye signs (including involvement of the pupils and extra-ocular muscles), 56 per cent; rash, 53.3 per cent; preceding upper respiratory symptoms, 30 per cent; swollen inflamed joints, 16.6 per cent; paralysis of an extremity, 3.3 per cent.

The earliest admission was six hours after the onset of symptoms; the latest, twenty-two days after onset.

Three children developed sequelae: In case 5, the patient developed bilateral deafness, in case 13, mental changes associated with hydrocephalus of the hypersecretory type (later died), and in case 17, bilateral internal strabismus.

SEROLOGY

The highest cell count in the spinal fluid in this series was 160,000; the lowest count at its peak was 74. Both of these patients died. The spinal fluid of the second patient was cloudy, showing countless meningococci in the direct smear. The infection was overwhelming, and the patient died fifteen and one-half hours after the onset of symptoms. The average polymorphonuclear percentage in the spinal fluid was 85; the average lymphocyte count, 15 per cent. A positive culture of meningococci was obtained from all cases except case 12. This case was accepted as one of meningococcus meningitis because of definite though mild symptomatology, and because three sisters with which this girl had been sleeping at home had died of this disease during the preceding month.

The average highest leukocyte count in the blood stream was 13,800, with 76 per cent polymorphonuclear cells, indicating a marked relative increase in view of the age incidence Following the initial high mortality in our series, an endeavor was made to determine the strain or strains of meningococci responsible for the small epidemic. Strains were isolated from thirty-two cases during the late winter and spring months of 1928. All were type I meningococci, except one which was type II.

In seeking for a satisfactory serum, the agglutination test, being the most generally accepted laboratory test for the determination of the potency of a serum against a specific organism, was used (table 1). Agglutination tests were performed with twenty of the isolated strains of meningococcus against each of the serums used. The following are illustrative cases selected from this series. It should be noted that throughout serum 3 was uniformly of the highest titer, yet was not

effective clinically. In table 1, the agglutinin content of all serums was fairly uniform, but it was slightly higher for 3 and 5.

CASE 5.—This patient, aged 7 years, had the disease for twelve hours before treatment with serum 2 was instituted. Twenty-one doses were given intraspinously, three intravenously and six intramuscularly. The total amount of serum given was 600 cc. The patient was cured. The results of the tests are shown in table 1.

Difficulty encountered in the obtaining of sufficient serum 2 and *2a* for our needs forced us to use other serums and to search for another serum of satisfactory potency against the organism we were encountering.

All antimeningococcus serums for general use are supposed to be polyvalent and effectual against all strains of meningococci likely to be encountered in the area of their distribution. The type of meningococcus which was present in these cases is one for which all polyvalent

TABLE 1.—*Case 5, Type I Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	++++	++++	++++	++	—	—
Serum 2	++++	++++	++++	++++	++	—
Serum 2a	++++	+++	+++	++	—	—
Serum 3	++++	++++	++++	++++	+++	++
Serum 4	++++	+++	++	+	—	—
Serum 5	++++	++++	++++	++++	++	+
Serum 6	++++	++++	++++	++++	—	—

antiserums should contain curative substances. That five were sadly lacking in this respect is made evident by a study of the accompanying tables. A rather widely held belief is that the extent of effective polyvalency in a serum depends on the number of strains used. At one time as many as sixty were used in the preparation of some serums. The number has been reduced until the majority of producers of serum use only from thirteen to seventeen strains divided among four groups. The serums in the included list were prepared with the use of from thirteen to seventeen strains, except in two instances. These are serum 2 (including *2a*, a different lot of the same serum) and serum 6. Six strains were used in their production. Unfortunately for comparative purposes, antiserum 6 was used only once very late in the treatment of a patient.

In comparing the clinical results following the use of serums 2 and *2a* with the results following the use of the other serums, it would seem that there may be a loss in specificity against a certain strain when a large number of strains have been used in the production of a polyvalent serum. A serum must be specific for the strain of meningo-

coccus which it is combating in order to be of therapeutic value in a given case.[5]

The problem of determining the best method of preparing a serum of value against all strains of the meningococcus and parameningococcus is still unsolved.

Therapeutic monovalent serum as prepared by the Pasteur Institute and later by Gordon and others in England working under the National Research Council has been discarded from practical use because of the difficulty and delay in determining the type of organism present.[6]

Wadsworth[7] pointed out that the presence of a large number of strains decreased the potency of the serum against any single strain. He concluded that serum produced with the use of from four to six representative strains (at least one regular meningococcus strain, one parameningococcus strain and two intermediate strains) possessed the greatest potency against the largest number of strains.

Blackfan[8] mentioned an occurrence similar to ours during the World War when the serum treatment was temporarily discontinued in one of the armies because it was ineffective against the strain of meningococcus present during the epidemic then in progress.

Felix and Yunowich[9] also reported a series of cases from the Jerusalem Jewish Hospital in which three standard serums from three different countries failed to act effectively, but serums from the Rockefeller Institute and from the New York State Department of Health were effective.

Concentration of the antibody content of antimeningococcus serum is now being done by Banzhaf and Neal of the New York City Board of Health, but as yet insufficient statistics are available to draw conclusions as to the clinical results obtained in comparison with the usual polyvalent antiserum.

All agglutination tests in this study were carried out uniformly. The same suspension of organisms was used with all serums at the same time under the same incubation conditions, namely, at 56 C.

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5. Felix, A., and Yunowich, R.: The Importance of Polyvalence in the Use of Therapeutic Antimeningococcus Serum, J. Immunol. **9**:193 (May) 1924. Blackfan, K. D.: The Use of Antimeningococcus Serum in the Treatment of Epidemic Meningitis, J. A. M. A. **76**:36 (Jan. 1) 1921.

6. Amoss, H. L.; Gates, F. L., and Olitsky, P. K.: Simplified Production of Antimeningitis Serum, J. Exper. Med. **32**:767 (Dec.) 1920. Felix and Blackfan (footnote 5).

7. Wadsworth, A. B.: Comparison of the Potency of Polyvalent Antimeningococcus Serum Produced with Four and Six Representative Strains and that Produced with Sixty Strains, as Determined by the Agglutinin Titre, J. Exper. Med. **33**:107 (Jan.) 1921.

8. Blackfan (footnote 5, second reference).

9. Felix and Yunowich (footnote 5, first reference).

for three hours and then at icebox temperature for the remaining time. readings were taken at one, three and twenty-four hour intervals. In these tests the serum known as 3 stands out as a serum of very high agglutinin content against the twenty recorded strains. It equalled all other serums and in most instances surpassed them (tables 2 and 3). Though it was used only in three cases, which is a small number for observation, it lacked power to control the infection.

CASE 7.—The patient, aged 3 years and 3 months, had an illness of four days' duration before treatment was begun. Treatment consisted in thirteen intraspinal, two intravenous and nine intramuscular doses of serum 1, six intraspinal doses of serum 4, nine intraspinal and two intracisternal doses of serum 7, three intracisternal doses of serum 3 and three intracisternal doses of serum 2. Serum 2 was

TABLE 2.—*Case 7, Type I Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	++	+	±	—	—	—
Serum 2	++++	++++	++++	++++	++	—
Serum 2a	+++	+++	++	+	±	—
Serum 3	++++	++++	++++	++++	++	+
Serum 4	++++	+	—	—	—	—
Serum 5	++++	+++	+++	++	+	—
Serum 6	++++	++++	++++	++++	+	—

TABLE 3.—*Case 9, Type I Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	—	—	—	—	—	—
Serum 2	++++	++++	++++	++++	++++	±
Serum 2a	+++	++	+	—	—	—
Serum 3	++++	++++	++++	++++	++++	++++
Serum 4	+	—	—	—	—	—
Serum 5	++	+	—	—	—	—
Serum 6	++++	++++	+	—	—	—

given the last three days before death. The total amount of serum given was 480 cc. The patient was under treatment for twenty-seven days.

In the tests on this case, two serums stand out as of very low agglutinin content, serums 1 and 4, both of which were used in the treatment; however, serum 3 was likewise tried and was useless (table 2).

CASE 9.—The patient, aged 2 years and 11 months, was ill for four days before treatment with serum 1 was instituted. The patient received two intraspinal doses and one intramuscular dose of serum 1. The total amount of serum given was 55 cc. The patient died two days after admission to the hospital.

In the agglutination tests on this patient, no agglutinin reaction was noted with type I strain in serum 1. The agglutinin content was low in all serums, except in serums 2 and 3. Serum 1 was used without effect (table 3).

Serums 1 and 4 paralleled each other rather closely in their agglutinin content and also in their lack of curative properties (table 5). Serum 5 equalled the agglutinin content of serums 2 and 2*a* against most of the strains but was powerless to control the infection. Anti-meningococcus serums 2 and 2*a*, though not universally high in

agglutinin content against the infecting strains, was specific and curative in its action in all cases when administered early. No other serum appeared to contain curative properties against these strains. Against the strain of case 15, serums 2 and 2*a* contained a lower agglutinin content than all other serums, but it did not fail in its curative properties (table 6).

CASE 11.—This patient, aged 3 years and 7 months, had an illness of one day's duration before treatment was begun. Serum 3 was used for five days, with no improvement. Ten intraspinal, five intramuscular and one intravenous dose of serum 3 was given. Six intraspinal and seven intracisternal doses of serum 2 were given. The total amount of serum given was 580 cc. Improvement was noted on the seventh day, or two days after the patient received serum 2. The patient recovered.

TABLE 4.—*Case 11, Type I Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	+	±	—	—	—	—
Serum 2	++++	++++	++++	++	+	±
Serum 2a	+++	++	±	±	—	—
Serum 3	++++	++++	++++	++++	++++	+++
Serum 4	+++	++	+	±	—	—
Serum 5	++++	++++	+++	++	+	—
Serum 6	++++	++++	++++	++	+	—

TABLE 5.—*Case 13, Type II Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	±	±	—	—	—	—
Serum 2	++++	++++	++++	++++	++++	++
Serum 2a	++++	++++	++++	++++	++++	++
Serum 3	++++	++++	++++	++++	+++	±
Serum 4	++++	+++	±	±	—	—
Serum 5	++	++	++	+	±	—
Serum 6	+++	+++	+++	+++	—	—

In this case, the highest agglutination titer was noted with serum 3, but a progressively downhill course followed its administration, clinically and serologically. Following a change to serum 2, of lower agglutinin content, almost immediate improvement resulted and cure followed (table 4).

CASE 13.—The patient, aged 2 years and 4 months, was ill for six days before treatment was instituted. Serum 5 was used for five days; eight intraspinal, one intramuscular and one intravenous dose of the serum were given. Eight intraspinal doses of serum 2 were then given. The total amount of serum given was 360 cc. The patient was cured. This patient later returned to the hospital, where she died from an internal hydrocephalus.

In this case, no improvement was noted during the five days that serum 5 was used; almost immediate change for the better followed when serum 2 was given, which was of higher agglutinin content (table 5).

CASE 15.—This patient, aged 20 months, had an illness of two days' duration before treatment with serum 2 was started, Sixteen doses were given intraspinally; the total amount of serum used was 320 cc. The patient was cured.

The agglutination test, although widely accepted as an index to the curative value of a serum, seems entirely inadequate in the light of the foregoing experience in the determination of the value of a serum against a specific organism. This is not a new observation. Other methods, such as the opsonic index and the complement-fixation test, have not been of proved value in this determination.

We would suggest that all antimeningococcus serums for general distribution should be accompanied by a slip to be filled in by the clinician as to the outcome of the treatment and returned to the producer. It is only by such cooperation that one can hope for real

TABLE 6.—*Case 15, Type I Strain*

Serum Dilution	1:20	1:40	1:80	1:160	1:320	1:640
Serum 1	++++	++++	++++	++++	++	—
Serum 2	++++	++	+	+	+	—
Serum 2a	+	+	+	—	—	—
Serum 3	++++	++++	++++	++++	++++	++++
Serum 4	++++	++++	++	++	—	—
Serum 5	++++	++++	+++	+++	++	++
Serum 6	++++	++++	++++	++++	++++	++++

TABLE 7.—*Results Following the Administration of the Various Serums*

Number of Cases	Types of Serum Used	Deaths	Cures	
5	1	5	0	
1	1, 3, 4, 6 and 2 (after 3 weeks)	1	0	
1	1-4	1	0	
2	5 (6 days) then 2 (4 days)	2	0	
1	3	1	0	
		10	0	100 Per cent mortality
1	3 (6 days) 2	0	1	
33	2-2a	4	29	
		4	30	12 Per cent mortality 88 Per cent cure

improvement in the product. The treatment for cerebrospinal meningitis is one of the few outstanding successes of serum therapy. The serum is depended on as a specific curative agent, which indeed it can be, as shown by the results obtained by the use of serums 2 and 2*a*.

TREATMENT

An analysis of table 7 shows that fourteen of the forty-four patients presented in this series died, and thirty were discharged as cured. A study of the serums used shows that all patients treated throughout by serums other than serums 2 and 2*a* died, whereas all patients treated by serums 2 and 2*a* alone were cured, except 4, two of whom were admitted to the hospital in a moribund condition; the other two died of a

complicating pneumonia. Four patients were treated first by other serums and later by serum 2; only one of these patients recovered. The late shift to serum 2 in these cases was due to a temporary inability to secure sufficient serums 2 and 2*a* for our needs.

These results emphasize the importance of not accepting a conclusion that a certain strain of meningococcus is resistant to serum treatment in either individual or epidemic cases. One can justifiably conclude only that the strain of meningococcus in question is resistant to the serum used, and try other serums. In the majority of the patients who were cured, improvement was noted within one week, and in all within two weeks of the beginning of treatment.

The therapeutic test appears to be the only accurate method of determining the value of the serum to be used.

THE TECHNIC OF ADMINISTRATION

The technic with which we treated the patients in the series herein reported gradually evolved as our results varied following the use of different serums. The first patients received the usual daily dose of serum given intraspinously. The succeeding patients were treated with increasing vigor as the impotency of the serum became more evident until we were giving serum intraspinously, intravenously and intramuscularly, two and often three times a day. When we were able to secure serum 2, which was efficacious but limited in amount, we found that we could get excellent results by injecting intraspinously alone, once a day. Cisternal punctures with injection of serum into the cisterna magna were routine when a blockage of the spinal canal was evident.

Earlier authors[10] advocated ventricular punctures to insure the serum reaching the ventricles when a blockage of the spinal canal occurred. Such a procedure is relatively simple in infants when the anterior fontanel is open, as in the case mentioned by McLean and Caffey.[11] In patients whose anterior fontanel is closed, the cisternal puncture is now generally accepted as the method of choice. This has been regarded as a rather dangerous procedure, but more than seventy-five cisternal punctures were performed by the members of the house staff of the Post-Graduate Hospital on these and other patients within four months without a single death which could be attributed to this procedure. When it is considered that these patients

10. Fischer, L.: Drainage of the Ventricle, Saline Irrigation-Injection of Antimeningitis Serum (Flexner) in Cerebrospinal Meningitis, Internat. Clin. **20**: 147, 1910. Lewkowiz, K.: Antiserum Treatment of Epidemic Meningitis, Arch. de méd. d. enf. **27**:193 (April) 1924; abstr., J. A. M. A. **82**:1821 (May 31) 1924.

11. McLean, S., and Caffey, J. P.: Sporadic Meningococcus Meningitis, J. A. M. A. **87**:91 (July 10) 1927.

were the most seriously ill, and that many of them were in a moribund condition, it is evident that with proper technic the cisternal puncture is not an especially hazardous procedure. Hence it should be used when indicated without hesitancy.

It is generally accepted that the amount of serum injected into the spinal cord or cisterna magna should be less by at least 3 or 4 cc. than the amount of cerebrospinal fluid withdrawn. Flexner,[12] in 1913, quoted Cushing in warning against increasing the intracranial pressure; "the medullary center of respiration already impaired from compression endures an additional burden less well than a medulla not so embarrassed." Koplik early realized this danger and advised the injection of serum only by the gravity method.

Case 12 of this series illustrates this danger. Through miscalculation the amount of serum injected exceeded the amount of cerebrospinal fluid withdrawn by 3 or 4 cc. Immediately there was a cessation of respiration and all audible and palpable evidence of heart action. Two needles were inserted into the spinal canal to insure rapid reduc-

TABLE 8.—*Average Amount of Serum Used in Patients Successfully and Unsuccessfully Treated*

	Average Cc. of Serum Used
Patients who died after use of unsatisfactory serums	323
Patients who were cured following the use of serum 2 and 2a	245

tion of intracranial pressure, and 5 cc. of epinephrine was injected directly into the left ventricle of the heart.

Such artificial respiration was used as could be instituted with the needles in position, and after an interval of two minutes the patient began to breathe and the heart action was again perceptible. She was so entirely recuperated as to eat heartily of the next meal, and was discharged shortly afterward as cured.

The gravity method of administration of any serum intraspinously has proved in our experience to be the safest technic.

Our average single dose of antimeningococcus serum was 20 cc. in all cases in which we were able to withdraw more than 20 cc. of cerebrospinal fluid.

The last patients of this series received only one injection in each twenty-four hours. The results were fully as good as with multiple injections (table 8). In making the estimates for table 8, patients were not included who died within twenty-four hours of admission. The patients who died received more serum on an average than those

12. Flexner, Simon: Accidents Following the Subdural Injection of the Antimeningitis Serum, J. A. M. A. **60**:1937 (June 21) 1913.

who lived, in spite of the fact that death frequently curtailed treatment (table 8). Potency of the serum, rather than the frequency of injections, proved to be the essential factor for successful treatment. Koplik [13] warned of the seriousness of meningitis in early infancy. It is worthy of note that our two youngest patients, each 3 months old and each treated with serum 2, were discharged as cured.

CONCLUSIONS

1. The agglutination test does not give uniform results, and is unreliable as a guide for determining the value of a certain serum against a specific strain of meningococcus.

2. As other methods such as the opsonic index and the complement-fixation test have not been of proved value in this determination, the therapeutic test appears to be the only reliable method of determining the curative value of a serum against a specific organism.

3. This test may result in fatality in the treatment in an individual case; yet it is invaluable, as in our experience, in the treatment in a series of cases.

4. When a patient with meningococcus meningitis fails to respond to treatment, one cannot justifiably conclude that the strain of organism encountered is resistant to serum therapy, but only that the serum used is not specific for that organism. It is necessary then to seek an effective serum.

5. There appears to be a loss in specificity against a certain strain of meningococcus when too large a number of strains have been used in the production of a polyvalent serum.

6. A single intraspinous injection of 20 cc. of an effective antimeningococcus serum in each twenty-four hours was therapeutically adequate. Potency of the serum rather than frequency of injections proved to be the essential factor for successful treatment.

7. The quantity of serum administered should, in general, be less by at least 3 or 4 cc. than the quantity of spinal fluid withdrawn.

8. Antimeningococcus serum should be administered cisternally when there is evidence of blockage in the spinal canal. With correct technic this is not an especially hazardous procedure.

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13. Koplik, Henry: Meningitis of the Epidemic Type in Children Below 2 Years of Age, J. A. M. A. **60**:1755 (June 7) 1913.

INFANTILE PYLORIC OBSTRUCTION

PRELIMINARY REPORT OF ITS ALLERGIC NATURE *

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In spite of much clinical observation, infantile pylorospasm and pyloric stenosis remain obscure in etiology and in their relationship to each other. Those observers who claim to be able to differentiate between them clinically, by roentgen examination or by both methods, are frequently proved wrong by the clinical course, at operation or at autopsy. Most clinicians include patients with both conditions in the classification of hypertonic infants, since general muscular hypertonus occurs with great frequency in them. Ward,[1] who reviewed this subject in 1927, inferred that the only way to differentiate between them is by the end-result. If, on the administration of atropine and on a thick diet, the child improves, the case is one of pylorospasm; if no improvement follows these measures or if the symptoms continue to grow worse despite them, a diagnosis of organic obstruction is made and operation is advised. At operation a firm muscular mass is found at the pylorus, partially or completely occluding it. The organic change is in itself usually insufficient to cause complete obstruction, but spasm of the muscles and edema of the mucosa and submucosa act as adjuvants and complete it. This pathologic evidence is borne out by the clinical fact that most of these infants take food normally and show normal growth curves for from a few days to a few weeks, when suddenly the symptoms begin. Something of an acute nature must have completed the preexisting partial obstruction. The proportion of functional and organic pathologic change varies in each case and is difficult to determine even by morphologic study. It is therefore advisable to consider both of these types of cases under the heading of "Infantile Pyloric Obstruction."

From the foregoing summary it can be seen that the vomiting and visible peristalsis common to this disease result from pyloric obstruction, either completely spasmodic or combined organic and spasmodic in origin, with the symptoms following completion of the obstruction by the smooth muscle spasm with its accompanying edema and exudation.

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* Submitted for publication, May 25, 1929.

* From the Allergy Clinic of Mt. Sinai Hospital.

1. Ward, J. L.: The Hypertonic Infant with Special Reference to Pyloric Obstruction, Arch. Pediat. **44**:706, 1927.

Students of anaphylaxis produced experimentally in animals and of allergy as it occurs in man find that the characteristic physiologic pathologic change of the shock reaction consists of smooth muscle spasm, edema and exudation. In addition, Ecker and Biskind [2] have observed the rabbit's intestine in situ during anaphylactic shock and have noted localized smooth muscle spasms, and in some instances actual peristaltic rushes following the shock dose of horse serum.

A consideration of these points led us to study cases of infantile pyloric obstruction from the allergic point of view. Accordingly, a series of cases has been investigated as to: (*a*) the family history of allergy; (*b*) the presence of other allergic reactions in the patients either at the time of the pyloric obstruction or later in life; (*c*) the demonstration of specific skin reactions to definite allergens, and their transfer by the Prausnitz-Küstner [3] method from the patient to the skin of a normal adult, and (*d*) therapeutic testing by the dietary change based on the evidence obtained by the immunologic methods used.

Cooke and Vander Veer [4] have shown that allergic patients have an allergic family history in about 50 per cent of the cases and that nonallergic people have such a background in only 15 per cent of the cases. Our analysis of the histories of twenty-seven cases, obtained by personal interviews and questionnaires, shows a familial tendency in eleven, or 40.7 per cent.

Eczema, urticaria, angioneurotic edema, eruptions caused by drugs, asthma, hay-fever and vasomotor rhinitis are usually considered allergic manifestations. A study of these twenty-seven cases shows the presence of one or more of these conditions before the age of 12 in twelve patients, a total of 44 per cent.

We have been able to make accurate immunologic studies on six infants, on four at the time of the pyloric obstruction and on two later in life. In all four studied during the pyloric obstruction, we were able to demonstrate definite positive reactions either dermally or intradermally to egg, milk or cereals, and in three we succeeded in transferring the reacting antibody to the skin of a normal person by the method of Prausnitz and Küstner. In the two cases studied later in life, at 8 and 36 months of age, respectively, both infants had marked eczema; one we found sensitive to egg, the other to milk and from both positive transfers were obtained.

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2. Ecker, E. E., and Biskind, M.: Allergic Reactions of the Rabbit's Intestines During Anaphylactic Shock as Recorded Cinematographically, Arch. Path. **7**:391 (March) 1929.

3. Prausnitz, C., and Küstner, H.: Centralbl. f. Bakteriol. **86**:160, 1921.

4. Cooke, R. A., and Vander Veer, A.: Human Sensitization, J. Immunol. **1**:201, 1916.

In all methods of testing used in this study, those areas showing definite wheals with pseudopods were considered to show a positive reaction, but only in the presence of completely negative controls. More importance is paid to the presence of pseudopods than to the size of the reaction, as infants show comparatively smaller reactions than adults.

REPORT OF CASES

The following are typical histories.

CASE 1.—B. A., a second child, aged 6 weeks, had a normal birth and developed normally on breast feedings until the third week, when typical signs of pyloric obstruction began. His brother, aged 3 years, had an organic pyloric obstruction for which a pyloroplasty was performed. His mother had recurring attacks of urticaria. Intradermal tests with the proteins of cow's milk, egg and wheat revealed a slightly positive reaction to lactalbumin. Passive transfer to a known satisfactory normal person by the method of Prausnitz and Küstner revealed a good reaction to the lactalbumin. Under the administration of atropine and the feeding of lactic acid milk, the signs abated and the child began to develop normally.

CASE 2.—S. W., aged 3 years, was admitted to the hospital at the age of 3 weeks because of typical signs of pyloric obstruction, which developed while he was taking breast milk. Change of diet to dilute cow's milk and the administration of atropine controlled the symptoms, and he was discharged within two weeks. During his hospitalization it was noted that he had coryza, which the mother stated had been present almost since birth. This persisted despite vigorous treatment and was marked at the time of examination. A sample of blood was obtained, and passive transfer was attempted. A marked reaction to egg was obtained. Egg was then eliminated from the diet. The eczema disappeared completely within one month without any local treatment. It did not recur during the administration of the egg-free diet.

CASE 3.—M., aged 8 months, had vomited after feeding since the sixth week of life. At first the symptoms were severe, and a diagnosis of spasmodic pyloric obstruction was made. Under administration of atropine and dilute cow's milk the severity decreased, but there was some vomiting daily. Many changes in the diet were instituted, without complete relief from symptoms. When the child was 8 months old, a positive Prausnitz and Küstner reaction to lactalbumin was obtained. The mother had hay-fever and came from a family with a history of allergy. Boiling the milk to change the chemical composition of its proteins and to get rid of the lactalbumin produced relief which has lasted more than a year.

COMMENT

From the evidence presented, it is seen that allergy may be present and may be demonstrated immunologically in cases of infantile pyloric obstruction, and that the physiologic pathologic change in these cases is similar to that in allergy.

The work of Cooke and Vander Veer,[4] Coca[5] and his co-workers calls attention to the familial nature of allergy, and shows that there is

5. Coca, A. F.: Human Hypersensitiveness, in Tice: Practice of Medicine, Hagerstown, Md., W. R. Prior Co., 1924, pp. 342.

marked difference in the facility with which persons become sensitized. Those with a marked predisposition may well become sensitized during prenatal life if sensitizing doses of allergens reach them by way of the blood stream. There is evidence that common foods are absorbed in pure form from the gastro-intestinal tract, and that these substances may pass from the maternal to the fetal circulation unchanged.

Walzer,[6] in studying experimental urticaria, has demonstrated in a large number of persons, both adults and children, that egg and fish proteins will produce urticarial reactions in areas of normal skin previously sensitized by the intracutaneous injection of serum from a person sensitive to egg or fish after the ingestion of these foods by the person to whom the transfer has been made. Obviously, these foods have been absorbed unchanged from the intestinal tract, have passed by way of the blood stream to the passively sensitized area, and there produced a typical antibody-antigen reaction.

Ratner[7] has demonstrated experimentally that allergic antibodies can pass through the placenta of the guinea-pig and passively sensitize the offspring. He has also succeeded in administering the sensitizing dose of horse serum to the guinea-pig fetus by injecting the substance into the mother a few days before parturition, and has demonstrated that sensitization, which was not present at birth, developed within a period of one month. Thus, the guinea-pig fetus may be sensitized as the result of the sensitized state of the mother or may actually develop active sensitization as a result of the absorption of the allergen from the nonsensitive mother by way of the placenta. Ratner further stated that human beings and guinea-pigs have similar types of placentas in which the fetal and maternal circulations are separated by but one layer of cells. He presented evidence in human beings of the passage of antibodies and other substances from mother to fetus.

The only essential difference between those cases of pyloric obstruction which show hypertrophy and those which do not show it may be in the time of onset of sensitization and its duration.

Sensitization may occur as follows: (1) active sensitization in utero early in prenatal life, (2) active sensitization in utero late in prenatal life, (3) active sensitization after birth from a sensitizing dose received in utero or (4) active sensitization after birth from a sensitizing dose received after birth, and (5) passive sensitization in utero.

Patients with organic pyloric obstruction are probably sensitized in utero early in prenatal life. Repeated shocks probably occur during

6. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings, J. Immunol. **14**:143, 1927.

7. Ratner, B.: A Possible Casual Factor of Food Allergy in Certain Infants, Am. J. Dis. Child. **36**:277, 1928.

prenatal life with the resulting secondary hypertrophy. After birth the child may develop normally for a few days until it receives a dose of the specific allergen, and this institutes further spasms and edema with its resultant signs.

Spasmodic pyloric obstruction may be the result of sensitization by any of the methods mentioned. It is likely that most cases represent late intra-uterine sensitivity with shock doses reaching the sensitized area after birth or infrequently before birth.

Those cases which develop from four to six weeks post partum may belong to groups 3 and 4 suggested in the classification and, in rare instances, may represent shock reactions in a passively sensitized patient.

SUMMARY AND CONCLUSIONS

The following evidence showing that infantile pyloric obstruction may be an allergic phenomenon has been presented:

1. The pathologic condition in infantile pyloric obstruction is probably identical with that in allergy.

2. Evidences of allergy are present in the majority of cases of infantile pyloric obstruction.

3. Depending on the period in life at which sensitization occurs and the frequency and severity of the shock reactions, there may be pylorospasm with or without organic obstruction.

SPONTANEOUS HYPOGLYCEMIA IN CHILDHOOD*

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Three years ago, I reported under the title "Recurrent Vomiting" [1] a number of cases in which there was a greater or less degree of hypoglycemia. Since that time, I have had occasion to see four more such cases, two of them fatal.

REPORT OF CASES

CASE 1.—During infancy, a diagnosis of hereditary syphilis was made in D. S., a colored girl, aged 4 years, and the child was treated with a brand of sulpharsphenamine. The Wassermann reaction became negative by the end of the first course of six treatments, and thereafter remained negative. When she was 3½ years old, she had an attack of pneumonia which ran a short uncomplicated course. At this time her liver was found to be enlarged, but there was no mention of jaundice.

On June 24, 1926, she suddenly began to vomit and had diarrhea. The following day, she was unable to retain anything, and complained of abdominal pain at frequent intervals. She grew worse, vomiting frequently, becoming more and more drowsy and paying no attention to what went on about her. She was admitted to the hospital on June 28. She was semicomatose, with rapid, irregular, shallow respirations. She cried out with apparent pain when the liver was palpated. There was evidence of consolidation in the right axilla. The liver was greatly enlarged, with a firm, smooth edge, and was tender. The spleen was barely palpable. The reflexes were sluggish. There was a pronounced odor of acetone in the breath.

The blood sugar on admission was 50 mg. per hundred cubic centimeters (Bang method). The spinal fluid showed 2 cells per cubic millimeter; the Pandy reaction was negative. The patient died a few hours later. At autopsy, the liver was found to be the seat of a diffuse fine scarring, intralobular in type. The surviving cells were filled with fat. There were also a few small epicardial hemorrhages. There was some fatty change in the kidneys. The pancreas and suprarenals were normal.

The mother said that the child had been seen with a variety of firecracker called "splitting devil" in her mouth a few hours before the onset of the disease, but she did not think that the child had swallowed any of it.

CASE 2.—The personal history of D. G., a white girl, aged 6½ years, had no apparent bearing on the attack to be described, as she had always been healthy and well developed. The onset occurred on July 7, 1925, at 3 a. m., with a complaint of abdominal pain. The child remained drowsy but was conscious for the next twenty-four hours and did not complain of pain. During this time, she took only about a glass and a half of milk. On July 8, she awoke with a violent headache. She vomited a little mucus. Four hours later, she had a convulsion

* Submitted for publication, May 4, 1929.

* From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics of the Johns Hopkins Medical School.

1. Josephs, H.: Recurrent Vomiting, Am. J. Dis. Child. **31**:657 (May) 1926.

and became unconscious. On admission, she was having occasional muscular twitchings of the face and arms. There was moderate jaundice. The pupils were widely dilated but reacted to light. The lungs were clear. The liver was greatly enlarged, with a firm, smooth surface and edge. Reflexes were not obtained. The temperature was normal and the pulse rate, 140. The spinal fluid showed 7 cells per cubic millimeter. The Pandy reaction was negative. The blood sugar (Bang method) was 48 mg. per hundred cubic centimeters. The carbon dioxide combining power of the serum was 28 per cent by volume. The inorganic phosphorus of the serum was 1.5 mg. per hundred cubic centimeters. Dextrose was administered by rectum without result, and three hours later the child died. The blood sugar content just before death was 45 mg. per hundred cubic centimeters. Urine was not obtained.

The autopsy showed extreme fat accumulation in the liver and kidney and small hemorrhages about the arch of the aorta and on the epicardium. No history could be obtained that the child had eaten anything that might contain phosphorus; but the closeness of the onset to the Fourth of July considered in connection with the condition found at autopsy makes phosphorus poisoning a strong possibility.

CASE 3.—M. M., a colored girl, aged 4 years, was entirely normal up to the time of the onset of the attack to be described. On Aug. 3, 1926, the child complained of pain in the neck. The next morning she awoke, apparently well, but ate little breakfast. At 11 a. m. she became unconscious, and shortly after that she had a convulsion which consisted of stiffening of the body without twitching. On admission to the hospital on August 4, one hour after the convulsion, the child was semicomatose. No hyperpnea was present. The pupils were contracted. The pharynx was deeply injected and the cervical glands enlarged. The liver and spleen were not palpable. The reflexes were sluggish. There was a marked odor of acetone in the breath. Shortly after admission, the child became conscious and by the next morning was only slightly drowsy. Improvement was rapid and by August 5, she was well.

Blood sugar estimation done on admission showed a content of 52 mg. per hundred cubic centimeters and four hours later, 56 mg. per hundred cubic centimeters. The blood sugar content on August 5 was 96 mg. per hundred cubic centimeters. No dextrose was given following admission, because of the marked clinical improvement.

It is probable that this reaction accompanied the onset of the rather mild pharyngitis. There is no reason to believe that there was any poisoning.

CASE 4.—W. B., a white girl, aged 7 years, since infancy had had spells of vomiting occurring about three or four times a year. All the attacks were similar. The onset in each case began with headache occurring early in the morning before breakfast; she soon began to vomit and for three or four days vomited everything she consumed; then the attack passed, and she was well until the next attack.

The onset occurred on Sept. 17, 1928, with severe frontal headache soon followed by vomiting. She appeared to have fever by that evening. The next day she became drowsy. She ate an ice-cream cone and vomited only twice, but she seemed no better.

On admission to the hospital on September 19, there was little to be found besides the evident somnolence and dehydration. Respiration was regular and deep. The tonsils were inflamed. The blood sugar on admission was 40 mg. per hundred cubic centimeters. The urine contained acetone bodies in large quantities.

Dextrose was administered intravenously, and thereafter she was given orange juice by mouth. Her drowsiness persisted for about eighteen hours after admission,

Principal Clinical and Laboratory Data in Ten Cases Showing Hypoglycemia

Name	Age	Attacks Repeated	Precipitating Factor	Fasting Period, Duration in Hours	Onset	Blood Sugar, per Cent	Symptoms	Duration	Comment
D. G.	6½	0	?	0	Gradual abdominal pain	0.048	Coma, headache; vomiting once; convulsion after 24 hours	36 hours	Died; autopsy: fatty liver and subepicardial hemorrhages; possibly phosphorus poisoning; serum phosphorus, 1.8; jaundice; carbon dioxide capacity of serum, 22 per cent by volume
D. S.	4	0	?	0	Abrupt with vomiting and diarrhea	0.050	Coma; vomiting; jaundice	4 days	Died; autopsy: fatty liver with intralobular scar tissue; subepicardial hemorrhages; possibly phosphorus or some allied poisoning
M. M.	4	0	Infection	0	Abrupt with unconsciousness and convulsions	0.052	Convulsions; marked drowsiness	1 day	Spontaneous recovery rapid
W. B.	3	+	?	12	Abrupt	0.045	Vomiting; drowsiness; ketosis	3 days	
N. H.*	2	+	Infection ?	18	Abrupt with convulsions	0.060	Convulsions; drowsiness; acetone bodies	2 days	Two previous attacks with vomiting commencing after a short fasting period (12 hours)
R. H.*	2½	0	Infection	0	Increasing drowsiness	0.058 after 3 days	Drowsiness; vomiting; convulsions after 3 days; acetone bodies	3 days	Slight acidosis; carbon dioxide capacity of serum, 28 per cent by volume; inorganic phosphorus of serum, 1.9 mg. per 100 cc.
L. S.†	2½	++	Infection usually Exhaustion from play once Fasting alone once Infection High fat diet once	.. 8 18 12 0	Abrupt with convulsions and vomiting	..... 0.045 0.036 0.052	Drowsiness; vomiting; convulsions; ketosis	1 to 3 days	Recovery rapid after administration of dextrose; spontaneous recovery after 3 days usually
S. E.*	7	++	1. Excitement 2. Infection 3. Infection	8 18 2	.....	..... 0.065 0.077	Drowsiness; vomiting; convulsions; ketosis; meningeal symptoms	1 to 3 days	Recovery rapid after administration of dextrose; many previous vomiting attacks without convulsions
S. S.†	7	++	Highly neurotic child, precipitating factor unknown	?	Abrupt with vomiting	1. 0.060 2. 0.072 3. 0.081	Vomiting; ketosis	3 to 4 days	Attacks probably of neurotic origin, less tendency to hypoglycemia as child became older
A. U.‡	7	0	Anesthesia	20	Gradual drowsiness and vomiting	0.060	Drowsiness; vomiting; convulsions	8 hours	Rapid recovery after administration of dextrose

* Josephs, H.: Am. J. Dis. Child. **31**: 109 (Feb.) 1926.
† Ross and Josephs: Am. J. Dis. Child. **28**: 447 (May) 1924.
‡ Josephs, H.: Bull. Johns Hopkins Hosp. **37**: 376, 1925.

but she did not vomit during this time. Forty-eight hours after admission, she was eating regularly again.

The blood sugar content two weeks after admission, estimated in the morning when the patient had not had breakfast, was 73 mg. per hundred cubic centimeters.

CLINICAL DESCRIPTION

I have summarized in the table the principal clinical and laboratory data in all the cases that I have reported up to the present in which hypoglycemia was actually found during the course of the attack. (This table includes, therefore, six cases previously reported.[2])

The principal symptoms were somnolence, which in severe cases might amount to coma, ketosis, vomiting and convulsions. Headache was somtimes complained of, abdominal pain occasionally, and once the clinical picture closely resembled that of meningitis. In the majority of cases the attack was precipitated by an acute infection, so that it is difficult to separate the symptoms of the acute infection from those of the hypoglycemic attack. The onset was usually abrupt and often occurred in the morning before breakfast or after a short period of anorexia, so that one may speak of a period of relative fasting preceding the attack. In several of the children the attack began with convulsions and thereafter changed into a condition of somnolence; one fell asleep at 11 a. m., after playing normally all morning, and at noon was feverish and comatose; another became gradually more and more drowsy during an infection, vomited repeatedly, and after three days began to have convulsions. Vomiting was common and varied considerably in type. A child might vomit in one attack and not in the next when the attacks were repeated. Vomiting might occur once at the onset or it might be uncontrollable throughout the attack, though uncontrollable vomiting was rare. Convulsive seizures were quite as common as the vomiting, but clonic convulsions were rarely seen. What occurred under observation was twitching of the extremities or facial muscles or a stiffening of the body with tremor of the extremities. The convulsions, while alarming in themselves, were not necessarily evidence of a severe attack. Little need be said of the ketosis, except that it was invariably present to a greater or lesser extent. There was no clinical evidence of acidosis except in two cases, and the carbon dioxide capacity of the serum confirmed the clinical impression in both cases. In the two cases in which it was determined, the inorganic phosphorus content of the serum was considerably reduced.

In regard to the blood sugar values, only a few words need be said. The method used was the Fitz modification of the old Bang method

2. Ross, S. G., and Josephs, H.: Metabolism of Recurrent Vomiting, Am. J. Dis. Child. **28**:447 (May) 1924. Josephs, H.: Bull. Johns Hopkins Hosp. **37**: 376, 1925; Fasting as Cause of Convulsions, Am. J. Dis. Child. **31**:169 (Feb.) 1926.

involving iodemetric titration of the reduced copper solution, and the values obtained on normal persons varied between 0.09 and 0.12 per cent, and tended to remain surprisingly constant in the same person. With this method I have not seen the wide variations that have been reported by others when making a series of estimations of blood sugar, and so I have accepted as significant values that might appear to be within normal limits to those whose use of a different method has given them a different experience.

ETIOLOGY

If one turns now to a consideration of the factors contributing to the onset, one finds that in the majority of cases the attack occurs at the beginning, or occasionally during the course of an acute infection. There are, however, other factors present at times, such as unusual excitement, exhaustion from hard play or ether or chloroform anesthesia. In addition to those factors there is often present also a fasting period which may not be more than that present in every person's life from supper to breakfast. In only two cases have I seen a fasting period alone preceding the onset of an attack (in L.S., a child with an extraordinary labile blood sugar and in W.B.).

The part taken by hard play in the reduction of blood sugar is not difficult to understand, and if the play is carried to the point of exhaustion, the body's available reserve of carbohydrate may be seriously reduced, with a consequent fall in blood sugar content. Such a fall in blood sugar has been found in Marathon runners, especially those who were most exhausted.[3]

In respect to anesthesia, the relation is not so evident. I studied a series of children who underwent short periods of ether anesthesia for tonsillectomy.[4] In every case there was a fall in blood sugar content from eighteen to twenty-four hours after the operation. In most cases, this fall was preceded by a rise lasting a few hours. Accompanying the fall in blood sugar was an increasing output of acetone bodies. I studied the respiratory quotient in a number of the children and found a curve that was closely parallel to the curve of blood sugar, so that it is probable that there is an increased use of carbohydrate during the first few hours after ether anesthesia. In the case of A. U., reported in the same paper, the blood sugar showed a tendency to fall even before the operation, after only a sixteen hour fast. There was a marked rise in blood sugar for several hours following the operation, accompanied by a similar rise in the respiratory quotient, but twenty-four hours later, the

3. Levine, S. A.; Gordon, B., and Derriek, C. L.: Some Changes in Chemical Constituents of Blood Following a Marathon Race, J. A. M. A. **82**:1778 (May 31) 1924.

4. Josephs (footnote 2, third reference).

blood sugar content reached 60 mg. per hundred cubic centimeters, a point lower than in any of the other children studied. At this point the child became drowsy, the odor of acetone in the breath became more pronounced, the acetone bodies in the urine increased tremendously, and she began to vomit.

It was not feasible to study the onset of an acute infection or a period of excitement for the effect on carbohydrate metabolism, so that I have no figures available to show what factors cause reduction in blood sugar in the great majority of cases. I shall return to the question of etiology after a discussion of the fatal cases.

PROGNOSIS AND TREATMENT

The prognosis is in general good, and there is a tendency to spontaneous recovery. This statement, of course, does not apply to those cases in which there is extensive damage to the liver, but, judging from the experience of McIntosh,[5] even in these cases continued injection of dextrose offers a possibility of cure. The tendency to spontaneous recovery was shown well by L. S. (presented in a previous report [6]) and by M. M. whose blood sugar content returned to normal during a period in which no food, not even dextrose, was given. Prognosis, however, is so bound up with the treatment that the two can be discussed only together.

The treatment for the attack consists in the administration of dextrose, and in one or two cases the results of an injection of dextrose by rectum or intravenously have been obtained as rapidly as in hypoglycemic shock due to insulin. L. S. and N. H. are examples of this. Often, however, the results of the giving of dextrose were somewhat disappointing, and recovery was slow even when the blood sugar content was raised. It cannot be assumed, however, that a single injection of dextrose will cause more than a temporary rise in blood sugar. In the case of S. E., who had a blood sugar value of 60 mg. per hundred cubic centimeters on admission, a determination made two hours after an intravenous injection of dextrose showed no change in blood sugar, but the next morning the patient had recovered spontaneously. I would consider, therefore, that frequently repeated small doses were of greater efficacy than single large doses every four hours. A child who does not vomit can take dextrose by mouth in orange juice, and even one who does vomit can frequently sip the orange juice without precipitating a vomiting spell. The use of a stick of candy has its merits, a method that has been used in the treatment for attacks of recurrent vomiting. It has also been noticeable that dextrose given at the onset is more apt to be

5. McIntosh, R.: Acute Phosphorus Poisoning, Am. J. Dis. Child. **34**:595 (Oct.) 1927.

6. Josephs (footnote 2, second reference).

efficacious than dextrose given later. In the case of S. S., the attacks were probably neurotic in origin; the hypoglycemia was therefore only incidental and had nothing to do with the symptoms; it did not occur in the later attacks. Treatment in this case belongs to the realm of psychiatry.

Prophylaxis against the attacks is the simplest method of treatment, and in the cases that I have reported here has consisted in directions given to the parents not to allow the child to fast for a prolonged period. A half a glass of milk at bedtime has been sufficient in the cases of L. S., S. E. and N. H. to prevent the repetition of attacks. These are the only cases in this series in which repetition occurred which have been followed closely enough to judge of the results. Infections should be prevented, but unfortunately this is not always possible, and the next best thing must be attempted—abortion of the attack. Orange juice with sugar added was successful twice in the case of S. E. after she had begun to vomit and was becoming drowsy. Dextrose should be given prophylactically before operation. It seems hardly necessary to multiply examples. All that need be said is that a period of fasting should be avoided, and when a condition is present that might precipitate an attack the child should receive carbohydrate in some form fairly frequently until the danger of an attack is over.

PATHOLOGY

In the two fatal cases reported, the condition found was similar: extreme fatty change in the liver and kidneys and subepicardial hemorrhages. The clinical symptoms and pathologic changes were those of some profound intoxication such as occurs in acute phosphorus or chloroform poisoning. Similar pictures are also found in the reported fatal cases of recurrent vomiting. The relation between disease of the liver and recurrent vomiting has been the subject of several articles,[7] but it is in the reports of autopsies that one finds the best evidence for such a relation, and I shall review these in some detail.

The earliest autopsy to be reported was by Griffith in 1900.[8] The clinical description in the case tallies well with that of recurrent vomiting. At autopsy the only observation of any importance was an extreme accumulation of fat in the cells of the liver and kidney. In 1905, Langmead[9]

7. Lamaq-Dormay: Gaz. hebd. d. sc. de Bordeaux, March, 1903: cited from Marfan, Les vomissements periodiques avec acetonémie, ed. 2, Paris, 1926. Guérin, Thèse de Paris, 1905. Richardière: Arch. de méd. d. enf. **8**:127, 1905. Mauban: J. de méd. de Paris, 1909, cited from Marfan. Dorlencourt: Soc. de pediat. de Paris, November 15, 1921. Worster-Drought, C.: Proc. Roy. Soc. Med., sect. Dis. of Children, May 23, 1923.

8. Griffith, J. C. Crozer: Am. J. M. Sc. **120**:343, 1900.

9. Langmead, F.: Brit. M. J. **1**:350, 1905.

reported the second case, also one of true "recurrent vomiting," with almost identical pathologic changes. Swain,[10] in 1906, reported a fatal case, in which death occurred after six days of vomiting, during which time the child had a "peculiar odor to the breath" and large amounts of acetone in the urine. There had been no previous attacks. There was slight jaundice, and the liver was enlarged. The child died following an exploratory laparotomy, and at autopsy nothing was found except an extreme accumulation of fat in the liver. While chloroform poisoning cannot be excluded as the cause of death and fatty change in the liver, it is probably only a subsidiary cause. In 1907, Myers [11] reported a fatal case of vomiting with acetonemia in which there were convulsions shortly before death. There had been no recurrence in this case. The liver showed an accumulation of fat, but no other organ was examined. In the same year, Langmead [12] reported two more cases with autopsy. His first case was one of vomiting, coma and marked acidosis ending in death in a short time. There were no recurrences, unless one accepts as such one or two vague vomiting spells that had nothing in common with the final attack. His second case was that of a child who began with vomiting and abdominal pain, having had a similar attack one year previously. While the patient was under chloroform anesthesia, the abdomen was explored; the child died shortly after in coma with marked ketosis. In both cases the liver showed an extreme accumulation of fat. Nothing of an inflammatory nature was found in the abdominal cavity. At the same time, Langmead reported three cases of delayed chloroform poisoning, and commented on the similarity of these to cases of severe recurrent vomiting. In 1908, Guthrie [13] reviewed the whole question and pointed out the similarity between the attacks of recurrent vomiting and certain severe diseases of the liver: chloroform poisoning, phosphorus poisoning and acute yellow atrophy. On the basis of a review of the literature, he thought that recurrent vomiting was due to failure of liver function. Langmead thought that changes in the function of the liver were secondary to whatever it was that caused the recurrent vomiting. Later,[14] apparently he changed his mind and considered the liver insufficiency to be primary. There was never any tendency to regard the fatty changes as anything but secondary. In 1909, Jones [15] reported an autopsy in a case of "recurrent vomiting." In this case, there were no recurrent attacks. The onset was sudden with uncontrollable vomiting. Three days later there was opisthotonos and twitching of the hands and feet,

10. Swain: Bristol Med.-Chir. J. **24**:116, 1906.
11. Myers, A. W.: Arch. Pediat. **24**:914, 1907.
12. Langmead, F.: Brit. M. J. **2**:820, 1907.
13. Guthrie, L.: Brit. M. J. **2**:1158, 1908.
14. Langmead, F.: Practitioner **89**:24, 1912.
15. Jones, E. C.: Arch. Pediat., 1909, vol. 26.

which continued intermittently until death two days later. The child alternated between delirium and coma. At autopsy, an extreme accumulation of fat was found in the liver, together with infiltration of round cells and some necrosis. The thymus was said to have been enlarged, but its weight was not given. Moser,[16] in 1921, reported two cases with autopsy. In neither of these cases were there any previous attacks. Both showed the characteristics of an acute intoxication in the sudden onset, and the violent and persistent vomiting ending in death in coma. In one of the cases convulsions occurred. At autopsy in both cases an accumulation of fat was found in the hepatic cells, and in one a beginning increase of connective tissue. Furno,[17] in 1923, reported the case of a child of 7 years who up to the time of the fatal attack had been in good health. The onset was sudden in the early morning, with convulsions and coma. The temperature was not elevated; the pulse rate was 130; the pupils were widely dilated; the liver was greatly enlarged, and an acetone odor of the breath was present. He died shortly after the onset, and at autopsy there were found fatty degeneration of the liver and pancreas, a somewhat enlarged thyroid and a thymus weighing 36 Gm., which Furno considered to be slightly enlarged. The last case is one reported by Marfan.[18] It was from the practice of M. Oelsnitz, and it is not clear that Marfan ever saw the patient. Four children in a family were subjects of "recurrent vomiting." Two of them died. The case of one of these is reported in some detail. This child had had no attacks previously to the fatal one. The onset was sudden, with vomiting and ketosis. Hematuria and convulsions developed shortly before death. The autopsy showed fatty liver and kidney, together with small hemorrhagic spots in the mucous membrane of the stomach.

It is evident that the majority of these cases are not properly cases of recurrent vomiting in any strict sense. After all, "recurrent vomiting" can hardly be considered a disease; it is a clinical picture brought about by a large variety of causes, and it is the repetition of some effective cause, together with the "constitutional" tendency of certain children to the attacks, that is responsible for the recurrences. There are, however, certain intoxications that are capable of causing an attack in a child who has not shown any previous susceptibility, and in this category may be put phosphorus and chloroform poisoning. Recently, also, another type of intoxication has been described,[19] namely, white snake root poisonings,

16. Moser: Frankfurt. Ztschr. f. Path., 1921, vol. 23.

17. Furno: Riv. di clin. pediat. **21**:257, 1923.

18. Marfan, A. B.: Les vomissements periodiques avec acetonémie, ed. 2, Paris, 1926.

19. Bulger, H. A.; Smith, F. M., and Steinmeyer, A.: Milk Sickness and Metabolic Disturbances in White Snake Root Poisoning, J. A. M. A. **91**:1964 (Dec. 22) 1928.

which in the western part of this country is called "milk sickness." This poisoning causes anorexia, vomiting, ketosis, subnormal temperature, somnolence, trembling of the extremities and sometimes convulsions. Autopsy shows an extreme fatty change in the parenchymatous organs.

One finds, then, profound alterations in the liver accompanying the severe and fatal form of the clinical picture that I have described as characteristic of the hypoglycemic condition in children. It must be remembered, however, that other organs are probably also affected even when no anatomic changes are found at autopsy, and it would be premature to attempt to assign the cause of the clinical picture to the changes in the liver alone. Fatty change can at most be taken only as evidence of some intoxication, and it can hardly be viewed as evidence of profound change of any specific function of the organ. We can find better reason to indict the liver from a consideration of the relationship between hypoglycemia and disease of the liver.

RELATION OF LOW BLOOD SUGAR CONTENT TO LIVER DAMAGE

An examination of the literature shows a fairly constant relationship between disease of the liver and hypoglycemia. In 1911, Frank and Isaac [20] reported hypoglycemia after the administration of phosphorus to rabbits. Desqueroux,[21] in 1916, confirmed this observation. Williamson and Mann [22] did not obtain uniform lowering of the blood sugar content in dogs poisoned with phosphorus, but Bodansky [23] offered an explanation in the fact that with well nourished dogs the results were inconstant but when the dogs were poorly nourished, reduction in blood sugar was uniform. McIntosh [5] recently reported hypoglycemia of an extreme degree in a child of 16 months, who had been seen playing with a box of roach paste known to contain phosphorus. The patient was comatose and jaundiced, but there were no convulsions and no excretion of acetone bodies. Bodansky [23] demonstrated a fall in blood sugar content in dogs poisoned with chloroform. Stander [24] reported a case of hypoglycemia following delivery, which he attributed to the use of chloroform. Underhill [25] showed repeatedly that hydrazine, which he believed to be a specific liver poison, caused reduction of the blood sugar content in dogs and rabbits. Hypoglycemia has been demonstrated in acute yellow atrophy.[26] In white snake root poisoning, previously referred to, Bulger and Smith

20. Frank and Isaac: Arch. f. exper. Path. u. Pharmakol. **69**:274, 1911.
21. Desqueroux, J.: Rev. de méd. **39**:616, 1916.
22. Williamson and Mann: Am. J. Physiol. **65**:267, 1923.
23. Bodansky, M.: Am. J. Physiol. **66**:375, 1923.
24. Stander: Bull. Johns Hopkins Hosp. **35**:46, 1924.
25. Underhill, F. P.: J. Biol. Chem. **10**:159, 1911-1912 and many later articles.
26. Feigl and Luce: Biochem. Ztschr. **86**:48, 1918.

and Steinmeyer found hypoglycemia associated with marked ketosis in animals. It is hardly necessary to multiply examples, for it is evident from the foregoing statements that hypoglycemia is part of the picture of certain severe acute diseases of the liver, and it is probable that the liver insufficiency is responsible, although one cannot exclude the possibility that other organs may be involved.

RELATIONSHIP TO RECURRENT VOMITING

The similarity between the picture of the hypoglycemic attacks in my patients and that of the attacks of "recurrent vomiting" is evident, even when one takes into account the fact that both vomiting and recurrences were often lacking in my cases. It is the essential nature of the attack that is of importance, and a recognition of this is found in Marfan's recent review [18] when he speaks of the equivalent of the attack in which vomiting may be entirely lacking or of recurrent vomiting without recurrence. In removing my cases from the category of "recurrent vomiting," I am merely ceasing to apply a name that has become rather a scrap basket to receive miscellaneous cases characterized by repeated vomiting, in which no attempt is made to find the true cause of the condition. The truth is that "recurrent vomiting" has never been really defined; the textbooks describe what is called a typical case, but each author has allowed a wide margin for variations until the entire subject is hopelessly confused.

CONSTITUTIONAL FACTOR

The relation between the clinical syndrome and the hypoglycemia has already been partially discussed in the section under the heading, "Etiology," in which the relation of certain precipitating factors to the fall in blood sugar was dealt with. At that time I said nothing of the constitutional factor, and this factor must now be taken up.

By the constitutional factor I mean not only the tendency of certain children to repeated attacks or to an attack under conditions that in other children would not produce an attack. It is the common experience of those who have studied large series of children to find lower values for blood sugar in infancy during fasting and to find greater variation under different conditions, especially a lowering during fasting. As the child grows older, this lability disappears, and in adults it is rarely found, although it does occur.

In 1914, Hilliger [27] reported a case of "recurrent vomiting" in which be found a tendency toward a marked reduction in blood sugar on fasting. In 1921, Knoepfelmacher [28] reported another case in which there was some fall in blood sugar; but in neither of these two cases

27. Hilligen: Jahrb. f. Kinderh. **80**:1, 1914.

28. Knoepfelmacher: Monatschr. f. Kinderh. **21**:241, 1921.

were there sufficient controls, although the drop in Hilliger's case of from 0.14 to 0.07 was well beyond the limits of normal. L. S., whose case was reported in 1921,[6] showed an extraordinary tendency to a drop in blood sugar content, not only on fasting but on a sudden change to a ketogenic diet. In this series, R. H., S. E., and A. U. showed a tendency to a drop in blood sugar content which was greater than that found in a series of normal children. In other children, also, who had a tendency toward repeated attacks of vomiting or convulsions there was a low blood sugar on fasting.[29] From this I would conclude that the lability of the blood sugar, which is usual in infancy, may persist into childhood and may explain the constitutional factor in the hypoglycemic syndrome. I have discussed this in a previous article, to which reference may be made, so that it would be useless to repeat the discussion.

SUMMARY

I have reported a group of cases in which hypoglycemia of greater or less degree was found. These cases were characterized by attacks in which there occurred somnolence often verging on complete coma, ketosis, vomiting and convulsions. In about half the cases, the attacks tended to recur. Two of the attacks were fatal, and at autopsy the liver was found to be the seat of extensive fatty change. The clinical syndrome associated with the hypoglycemia has been the one usually associated with the term "recurrent vomiting." From a review of the literature, I have reason to regard the term "recurrent vomiting" applied to the reported fatal cases as a misnomer, since in the majority there were no recurrences, and in many vomiting was hardly more than incidental. In all the reported fatal cases there was marked fatty change, especially in the liver, as has been pointed out by others many times. Under experimental conditions, hypoglycemia has been associated with intoxications due to poisons causing profound anatomic changes in the liver, such as phosphorus, chloroform, hydrazine and white snake root. Hypoglycemia has been reported clinically in phosphorus and chloroform poisoning, and the clinical picture of these cases is closely similar to that of the cases reported and reviewed here. The tendency of certain children to hypoglycemic attacks has been ascribed to a lability of the blood sugar, which tends to fall more rapidly during a short period of fasting than is usual beyond the stage of infancy.

29. Josephs (footnote 1; footnote 2, fourth reference).

A WEIGHT RANGE TABLE FOR CHILDREN FROM 5 TO 15 YEARS OF AGE *

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In a previous paper [1] on variability of weight in relation to height in school children, attention was directed to the fact that the range of weight increases with age for both sexes, but more for girls than for boys and more on the overweight than on the underweight side, and that in consequence the customary static allowance of 7 or 10 per cent for underweight and of 20 per cent for overweight irrespective of age and sex is seriously misleading. Moreover, the determination of a single standard figure of weight for each unit of height, age and sex is somewhat uncertain and on the whole unsatisfactory, since (contrary to common opinion) there are usually more overweight than underweight children and average or mean weights of a given series are probably too high. This is best demonstrated by frequency curves which almost invariably show the mode [2] or peak at a point considerably lower than the mean. In table 1, the modes and means are given for six groups of children of like age, sex and height.

Considering the variables present, one is not surprised that tables of standard weights have to some extent fallen into disfavor with students of nutrition and workers in various fields of child hygiene. Certainly, it is no longer the best opinion that malnutrition should be diagnosed simply from an arbitrarily selected percentage deviation from a standard weight. The reaction has perhaps gone too far and the weight for the height been too completely disregarded. It has seemed to me that by utilizing the changing variables of age and sex, a table could be set up which would show, not the single "normal" weight for each unit of height, age and sex, but an approximately normal range of weight for

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* From the Department of Pediatrics, Stanford University Medical School, and The San Francisco Tuberculosis Association.

1. Faber, H. K.: Variability in Weight for Height in Children of School Age, Am. J. Dis. Child. **30**:328 (Sept.) 1925.

2. The mode is the figure attained by the largest number of individuals in a given series, and when there is a large element of uncertainty as to complete uniformity of material, it presents perhaps the most rational basis for a standard figure. It cannot, however, be determined with great exactness. In the tables here presented, it must not be assumed that the mode weight is midway between the upper and the lower figure of the range. Actually it is nearer the lower, but not by a uniform interval.

each unit, computed in such a way as to have a uniform significance in each case and that thus a still useful standard could be attained.

To this end, the weights of over 60,000 school children of San Francisco between the ages of 5 and 15 years were grouped according to height, age and sex; frequency distributions were made, the 10 and 90 percentile points determined, and a table constructed which for each unit of height, age and sex shows the approximate range of weight that would take in the central 80 per cent of cases. With such a table, underweight and overweight are defined as deviations from the normal greater than that of 90 per cent of the children of like height, age and sex. While drawing an arbitrary line (though not contrary to common sense), the method and the ranges apply with uniform significance to all ages and both sexes and set up no claim to greater pathologic significance than is implicit in such a degree of deviation. From such a table, no percentages of underweight or overweight can be calculated in the indi-

TABLE 1.—*The Modes and Means of Children's Weights at a Given Age and Height*

Age	Sex	Height	Weight		Cases
			Mode	Mean	
6	M	44	44.5	44.5	361
6	F	44	43.5	44.0	378
9	M	50	59.0	59.2	613
9	F	50	58.0	59.1	602
13	M	59	89.0	90.5	528
13	F	59	94.0	95.1	540

vidual case. To one familiar not only with the excessive labor of such calculations in school weighing but also with the repercussions of distress and indignation from children and their parents when overzealous teachers or school nurses have issued warnings of underweight or overweight on the basis of deviations of 1 or 2 pounds from the "standard," the omission is an advantage. The table of ranges permits a simple classification of the weight in the individual case as "within normal limits" or "outside normal limits." While the dividing line is still arbitrary, the allowance is sufficiently generous in both directions, and there is little doubt that a child exceeding the limit in weight requires medical examination.

To the objection that the table of ranges will allow many children really malnourished to escape attention, it is fair to reply that this is true of any method dependent on weighing and measuring alone. The health service of the modern school should use weight as only one of the methods of detecting ill health and that by no means the most important. Nor should any diagnosis of malnutrition be made on weight alone.

TABLE 2.—*Weight-Height-Age Table for School Children of California—Boys*

Height, In.	Normal Range of Weight, Lb.*										
	5 Yr.	6 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.
39	34-40	34-40	.....	.....	.....	.....	.....	.....	.....	.....	.....
40	35-41	35-41	.....	.....	.....	.....	.....	.....	.....	.....	.....
41	36-42	36-43	37-44	.....	.....	.....	.....	.....	.....	.....	.....
42	37-44	38-45	38-45	39-46	.....	.....	.....	.....	.....	.....	.....
43	38-45	39-46	39-46	40-47	.....	.....	.....	.....	.....	.....	.....
44	40-47	41-48	41-48	41-49	42-51	.....	.....	.....	.....	.....	.....
45	42-49	43-50	43-50	43-52	44-53	.....	.....	.....	.....	.....	.....
46	44-51	45-52	45-52	45-54	46-55	.....	.....	.....	.....	.....	.....
47	46-53	47-54	47-55	47-56	48-57	48-58	.....	.....	.....	.....	.....
48	.....	49-58	49-58	49-58	50-59	50-60	50-62	.....	.....	.....	.....
49	.....	51-60	51-60	52-62	52-62	52-63	52-64	.....	.....	.....	.....
50	.....	54-63	54-63	54-65	54-65	55-66	55-67	55-68	.....	.....	.....
51	.....	.....	57-66	57-68	57-68	57-69	57-69	57-71	.....	.....	.....
52	.....	.....	60-70	60-71	60-71	60-72	60-74	60-74	60-75	.....	.....
53	.....	.....	62-73	62-74	63-75	63-75	63-76	63-77	63-78	.....	.....
54	.....	.....	.....	63-76	64-77	64-78	65-80	66-81	66-81	66-82	.....
55	.....	.....	.....	65-78	67-80	67-81	67-83	68-84	68-85	69-86	.....
56	.....	.....	.....	.....	70-84	71-85	71-87	71-87	71-88	73-90	74-92
57	.....	.....	.....	.....	73-87	74-89	74-91	74-91	75-93	76-95	77-96
58	.....	.....	.....	.....	76-91	77-93	77-95	77-95	78-97	80-99	81-101
59	.....	.....	.....	.....	.....	80-98	80-99	81-101	82-102	83-103	84-104
60	.....	.....	.....	.....	.....	84-101	84-103	85-104	86-106	86-107	87-108
61	.....	.....	.....	.....	.....	.....	87-107	88-109	89-111	90-112	91-113
62	.....	.....	.....	.....	.....	.....	91-112	92-113	94-116	95-118	96-119
63	.....	.....	.....	.....	.....	.....	95-117	96-118	97-121	99-123	101-125
64	.....	.....	.....	.....	.....	.....	.....	99-122	101-125	104-129	106-131
65	.....	.....	.....	.....	.....	.....	.....	104-128	106-131	107-133	110-137
66	.....	.....	.....	.....	.....	.....	.....	.....	110-137	112-139	115-142
67	.....	.....	.....	.....	.....	.....	.....	.....	115-142	117-146	119-148

* The weights given represent the approximate permissible range for normal children. Underweight is calculated as pounds under the lower figure; overweight, as pounds over the higher figure. Percentages of under and overweight are not to be computed from these tables. Children whose weights are not within the given range should receive special study and attention. Children whose weights are within the given range are not necessarily free from physical defects, nor are the others necessarily physically defective.

TABLE 3.—*Weight-Height-Age Table for School Children of California—Girls*

Height, In.	Normal Range of Weight, Lb.*										
	5 Yr.	6 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	12 Yr.	13 Yr.	14 Yr.	15 Yr.
39	33-38	33-39	.....	.....	.....	.....	.....	.....	.....	.....	.....
40	34-41	34-41	.....	.....	.....	.....	.....	.....	.....	.....	.....
41	35-41	35-42	36-43	.....	.....	.....	.....	.....	.....	.....	.....
42	37-44	37-44	37-44	.....	.....	.....	.....	.....	.....	.....	.....
43	38-45	38-45	38-46	38-46	.....	.....	.....	.....	.....	.....	.....
44	40-47	40-47	40-48	40-48	.....	.....	.....	.....	.....	.....	.....
45	42-49	42-49	42-50	43-50	43-52	.....	.....	.....	.....	.....	.....
46	44-51	45-53	45-53	45-54	45-54	45-56	.....	.....	.....	.....	.....
47	46-53	46-55	46-55	46-56	46-57	46-58	.....	.....	.....	.....	.....
48	.....	47-57	48-58	48-58	48-59	48-60	49-62	.....	.....	.....	.....
49	.....	50-59	51-61	51-62	51-62	51-64	51-66	.....	.....	.....	.....
50	.....	53-63	53-63	53-64	53-66	54-67	54-69	56-72	.....	.....	.....
51	.....	.....	55-67	55-67	56-69	56-70	57-72	58-74	.....	.....	.....
52	.....	.....	58-71	58-72	58-72	58-73	59-75	59-76	.....	.....	.....
53	.....	.....	61-73	61-74	62-76	62-78	62-78	62-80	62-82	.....	.....
54	.....	.....	.....	63-77	64-79	64-81	64-82	65-83	66-85	.....	.....
55	.....	.....	.....	66-81	67-82	67-84	67-86	68-88	69-90	70-91	.....
56	.....	.....	.....	.....	70-86	70-88	70-90	71-92	73-95	74-96	.....
57	.....	.....	.....	.....	73-89	73-91	74-94	75-96	77-99	78-102	82-106
58	.....	.....	.....	.....	.....	76-95	77-98	78-100	80-103	83-108	86-111
59	.....	.....	.....	.....	.....	80-100	81-104	82-106	84-109	86-112	90-117
60	.....	.....	.....	.....	.....	84-105	85-108	86-110	87-113	90-117	95-123
61	.....	.....	.....	.....	.....	.....	89-114	90-116	91-118	94-122	98-128
62	.....	.....	.....	.....	.....	.....	94-120	95-122	95-124	97-126	102-132
63	.....	.....	.....	.....	.....	.....	.....	99-128	100-130	101-131	105-137
64	.....	.....	.....	.....	.....	.....	.....	103-132	104-135	105-137	108-140
65	.....	.....	.....	.....	.....	.....	.....	106-137	108-140	110-143	111-144
66	.....	.....	.....	.....	.....	.....	.....	.....	112-145	113-147	114-149
67	.....	.....	.....	.....	.....	.....	.....	.....	116-151	117-152	118-153

* Measurements are to be taken in indoors clothing, without shoes, coat or sweater. Heights are best taken with heels and head against a wall on which an accurate scale with half or quarter inch divisions has been marked or fastened. The head must be level and the body as erect as possible. The age is taken as that of the nearest birthday.

The present table was prepared for the San Francisco Tuberculosis Association and, approved by the Board of Health and Board of Education, it has been in use in the public schools of San Francisco for over three years. It has also been adopted by public schools and certain other institutions in other cities of California.

BACTEREMIA AND SKIN MANIFESTATIONS IN LIPOID NEPHROSIS *

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Lipoid nephrosis is now considered as a clinical entity. It is characterized by an insidious onset, usually without any evidence of a preceding acute infection. There is a chronic recurrent edema lasting a few days or a few months, with a marked tendency to remission. There is an increase in the lipoid and a decrease in the protein content of the blood. Occasionally skin lesions are seen. The etiology is not clear. Some writers state the belief that lipoid nephrosis is due to bacterial infection; others, that it is a purely metabolic disturbance affecting the entire body.

As shown by us in a previous paper [1] the prognosis of lipoid nephrosis is not good. A frequent cause of death is intercurrent pneumococcal peritonitis. In the present paper, nine cases of lipoid nephrosis in children are described; five of the patients died. These cases are interesting in that pneumococci or streptococci were repeatedly recovered from the skin lesions, the blood or the ascitic fluid. The accompanying table gives a summary of the observations.

The nine patients included five boys and four girls, from 2½ to 12 years of age. Six of these, at some time during our observation, showed one or more positive blood cultures. In one case a positive culture was obtained from an abscess in the skin, and in five cases there was a bacterial invasion of the ascitic fluid. In two of the cases here reported there was repeated invasion of the blood stream during the period of the illness; on two different occasions in one case, and on four in the other (cases 6 and 7). It is evident, therefore, that bacterial invasion is frequent during lipoid nephrosis.

REPORT OF CASES

CASE 1.—*History.*—R. S., a girl, aged 2½ years, who was admitted to the hospital on Aug. 20, 1922, had an unimportant family and past history. Three months before admission there was a gradual appearance of edema on the face and the extremities. The child became progressively more edematous and pale.

Examination.—The physical examination on August 25 showed: weight, 39 pounds (17.7 Kg.); general anasarca; small tonsils; normal eyes and ears; slight

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1. Schwarz, H., and Kohn, J. L.: Studies of Nephritis in Children: I. Nephrosis, Am. J. Dis. Child. **24**:125 (Aug.) 1922.

bilateral hydrothorax, and moderate ascites. The liver was palpable 1½ finger-breadths below the free border of the ribs; the spleen and kidneys were not felt. The blood count showed: white cells, 17,000, and polymorphonuclears, 59 per cent. The Wassermann reaction of the blood was negative. The blood chemistry revealed: urea nitrogen, 14 mg. per hundred cubic centimeters. The cholesterol content was 0.288 per cent, the serum being distinctly milky. Examination of the urine showed: specific gravity, 1.028; albumin in large amounts, and, microscopically, a few white cells, and hyaline and granular casts.

Course.—On August 30, the edema was about the same. The urine could not be measured because of the age of the child. The water test showed good power of concentration.

On September 4, the weight was 36 pounds (16.3 Kg.). The child was then on a high protein diet.

On September 11, the blood chemistry showed: urea nitrogen, 16 mg. per hundred cubic centimeters of blood, and cholesterol, 0.564 per cent; the total serum protein amounted to 7.1 per cent.

On September 12, the child suddenly became acutely ill with an inflamed throat and uvula. The temperature rose to 104 F. A blood culture showed a hemolytic streptococcus. The next day, there was a definite thin white exudate on the uvula; the temperature was still elevated.

On September 19, the urine showed a gram-positive organism which could not be cultured. A blood culture gave negative results and there still was fever. Although the temperature was gradually diminishing, the child's condition by September 28, was becoming rapidly worse; signs of peritonitis were growing more evident.

On October 2, aspiration of the peritoneal cavity revealed pus containing hemolytic streptococci. The next day, a laparotomy was performed, revealing a collection of pus in the peritoneal cavity. Soon after, the child died.

Autopsy.—The child was well developed and well nourished with no jaundice and no petechiae. There was no pretibial edema or edema of the face. In the hypogastrium there was a recent wound about 6 cm. in length.

The trachea contained a small amount of pinkish fluid and the mucosa was somewhat congested. The lungs together weighed 260 Gm. Both pleural sacs were free from adhesions and fluid. The surfaces were light pink. On palpation, they felt rather firm. Section showed a marked passive congestion. The blood-vessels and bronchi were normal.

The heart weighed 40 Gm. The pericardial cavity contained a slight increase of pericardial fluid. The fluid was light yellow and clear. The pericardial surfaces were smooth and glistening. The heart was light brown, the musculature on cut section showing no fatty change or fibrous streaking; there was no hypertrophy of either side. The valves were normal. The foramen ovale and the ductus arteriosus were closed.

A few coils of small intestine were adherent to the edge of the wound along the peritoneal surface. The retroperitoneal lymph nodes were enlarged and, on cut section, appeared slightly brownish.

The liver weighed 560 Gm. The surface was smooth and light brown. On cut section, the markings appeared to be somewhat obscured, and the surface was light brown. The central veins were made out with difficulty. The blood vessels were normal, as were the gallbladder and bile ducts.

The spleen weighed 33 Gm. The surface was covered by a thick purulent fibrinous exudate which was especially present over the anterior surface. The cut

Bacteriologic Examination of the Blood and the Ascitic Fluid

Patient	Date of Examination	Day of Fever	Blood: Culture and Organism	Blood: Number of Colonies per Cc.	Blood: Growth on Culture Mediums	Ascitic Fluid, Culture and Organism	Main Symptom at Time of Examination	Edema	Skin Lesion	Notes
1	9/12/22	1st	Hemolytic streptococcus	?	Fluid	.....	Pharyngitis	++	—	
	9/19/22	7th	Negative	..	.....	.....	None	++	—	
	10/ 2/22	16th	.....	..	.....	Hemolytic streptococcus	Peritonitis	++	—	Died
2	1/ 9/26	None	Pneumococcus type IV	70	Fluid and solid	.....	None	++	—	
	1/13/26	None	Negative	..	.....	.....	None	++	—	Improved
3	10/ 2/26	None	Negative	..	.....	.....	None	++	—	Improved
4	10/12/25	None	.....	..	.....	Negative	None	++	—	
	12/23/25	None	.....	..	.....	Negative	Erysipeloid	++	Erysipeloid of face	Improved
	1/ 7/26	1st	Pneumococcus type IV	4	Solid	.....	None	++	—	
	2/ 1/26	1st	Negative	..	.....	.....	Cough	++	—	Improved
5	5/10/24	7	.....	..	.....	Gram-positive coccus	Peritonitis	++	—	Died
6	7/24/24	3d	Pneumococcus type III	?	Fluid	.....	Peritonitis (?)	++	—	
	7/27/24	6th	Negative	..	.....	.....	Peritonitis	++	—	
	7/29/24	—	.....	..	.....	.....	Erysipeloid	++	Erysipeloid of face	
	8/10/24	—	.....	..	.....	.....	Abscess of the skin	++	Pus from abscess of skin showed pneumococcus type IV	
	4/13/25	1st	Pneumococcus type IV	5	Fluid and solid	.....	Erysipeloid	++	Erysipeloid	Died

7	6/23/25	—	—	..	.....	Negative	None	++	—	
	7/ 8/25	2	Pneumococcus type IV	3	Fluid and solid	.....	Abdominal pain	+	Erysipeloid	
	7/16/25	8th	Negative	..	.....	.....	Abdominal pain	++	Erysipeloid	
	1/12/26	—	Negative	..	.....	.....	Abdominal pain	+	—	
	1/19/26	—	.....	..	.....	Smear positive; culture negative	None	+	—	
	2/24/26	2	Negative	..	.....	.....	None	++	Papular eruption, remaining a few months	
	10/24/26	1	Pneumococcus type IV	4	Fluid	.....	Abdominal pain and erysipeloid	+	—	
	10/25/26	2	Pneumococcus type IV	4	Fluid	.....	Erysipeloid	+	Erysipeloid rash, 2 days' duration	
	9/30/27	None	Negative	..	.....	.....	None	+	—	
	9/30/27	None	.....	..	.....	Smear positive; culture negative	None	—	—	
	11/23/27	None	Negative	..	.....	.....	None	+	—	
	12/11/27	1	Negative	..	.....	.....	None	—	—	
	12/27/27	1	Hemolytic streptococcus	?	?	.....	Abdominal pain	+	—	
	12/29/27	3	Hemolytic streptococcus	1	Solid	.....	Abdominal pain	+	—	
	1/ 3/28	6	Negative	..	.....	.....	None	+	—	
	4/23/28	2	Pneumococcus type IV	32	Fluid and solid	.....	Peritonitis	+	—	Died
8	2/19/26	—	Negative	..	.....	.....	None	++	—	
	3/16/26	—	Negative	..	.....	.....	Erysipeloid	++	Erysipeloid	
	4/21/26	—	Negative	..	.....	.....	None	++	Erysipeloid	
	5/17/26	—	Negative	..	.....	.....	None	++	Erysipeloid	
	8/11/26	1	Negative	..	.....	.....	None	++	Erysipeloid	
	9/20/26	1	Negative	..	.....	.....	Bronchitis	++	—	Improved
9	12/24/27	2	Pneumococcus type IV	200	Fluid and solid	Pneumococcus type IV	Abdominal pain, peritonitis	++	—	Died

section showed marked congestion. The surface was deep red. The malpighian corpuscles could not be distinguished.

The suprarenal glands appeared to be normal.

Together, the kidneys weighed 200 Gm., having increased to about twice the normal size. They felt soft. The capsules stripped with ease, revealing numerous congested stellate veins but no evidence of hemorrhage into the cortex. The surface was light brown. The cut section showed marked swelling of the tissue. It was light brown. The markings were obscure. In some places the cortex and medulla appeared to merge, there being no line of demarcation. In other places the cortex and medulla seemed to be of normal proportions. The glomeruli could be distinguished only with difficulty. There were no hemorrhages into the cortex. Both pelves appeared to be dilated. This was especially true of the left kidney. On inspection of the ureters, no cause was found for this. The blood vessels did not stand out prominently and appeared to be soft.

The ureters and the bladder were normal, as was the pancreas.

The stomach was somewhat dilated. The mucosa was congested and was covered by a thick slimy exudate. The intestines, except for peritonitis on the serosa, were normal.

Microscopic Examination.—There was congestion and edema of the lung.

The capsule of the liver was markedly thickened owing to a thick deposit of fibrinopurulent exudate. The parenchyma showed marked cloudy swelling and fatty infiltration of the liver cells.

The malpighian bodies of the spleen were hypoplastic. The pulp showed congestion and cellular increase.

The kidney showed marked tubular degeneration which did not differ from that seen in many acute infections. There were some widespread areas of interstitial infiltration in both the cortex and the medulla consisting of polymorphonuclear and round cells. Many of the tubules were filled with leukocytes. Nile blue sulphate stain showed, in a moderate number of tubules, deposits of lavender stained material, some of which was in wandering cells and in the lumina of tubules. Several areas of scarring in the cortex contained these deposits.

CASE 6.—*History.*—S. M., a boy, aged 8, admitted on Nov. 20, 1921, presented an unimportant family history. The patient had had pneumonia and measles one year before. He had not had scarlet fever, but had frequently had tonsillitis. Six weeks before admission, he suddenly began to have general edema. No infection or fever was present. He had had marked oliguria for a few days.

Examination.—The patient was in a markedly edematous condition. He weighed 77 pounds (34.9 Kg.). The teeth were in poor condition. The tonsils were cryptic and hypertrophied. Dulness was observed at the bases of both lungs, with diminished breathing. The heart was normal. The abdomen was distended, disclosing a distinct fluid wave. There was general anasarca. The Pirquet reaction was positive. The blood pressure was 100 systolic and 80 diastolic. Examination of the urine showed: specific gravity 1.030, and albumin 2 plus. Microscopic examination revealed a large number of granular casts. Examination of the blood showed: leukocytes, 18,000, and polymorphonuclears, 74 per cent. The Wassermann reaction was negative. The blood chemistry showed: urea nitrogen, 19.6 mg. per hundred cubic centimeters of blood; cholesterol, 0.628 per cent, and serum protein, 4.2 per cent. The basal metabolism was minus 30 per cent.

Course.—On November 30, the patient was placed on a Karrell diet, 500 cc. of milk daily. There was no change in weight. The chloride test showed marked retention.

On December 3, a water test showed good concentration.

On December 12, the urea nitrogen amounted to 14 mg. per hundred cubic centimeters of blood; the cholesterol, 0.36 per cent; the total serum protein, 4.4 per cent, and the total serum fat, 1.3 per cent.

On Jan. 6, 1922, the water test showed an intake of 800 cc. The excretion in four hours was 680 cc., and in twenty-four hours, 950 cc.

On January 22, the patient weighed 55 pounds (24.9 Kg.). He was discharged as improved. Examination of the urine showed a large quantity of albumin. The cholesterol content of the serum was about normal.

On July 22, the patient was readmitted with a report that no edema had been noted from the time of discharge until three weeks before, when a gradually increasing anasarca appeared. Physical examination disclosed the condition of the nose and throat to be the same as on the previous examination. The heart and lungs were normal. The abdomen was rigid; there was tenderness in the right upper quadrant. The blood pressure was 105 systolic and 60 diastolic. Examination of the blood showed: polymorphonuclears, 23 per cent; eosinophils, 8 per cent, and lymphocytes, 60 per cent. The urine contained large quantities of albumin. The blood chemistry showed normal figures for nitrogen, and cholesterol 0.13 per cent. The serum protein was 6.3 per cent, and the serum globulin 2.65 per cent.

During his stay in the hospital, the patient gradually lost his edema. By August 15, the mononucleosis had disappeared, but the excretion of albumin continued.

On November 26, the patient was admitted for the third time, having shown no visible edema or subjective symptoms until two weeks before admission, when a slight cold was followed by a return of the edema. On physical examination, the patient weighed 82.5 pounds (37.4 Kg.). The throat was red, and there was generalized edema. Fluid was present at the base of both lungs, and there was a small amount in the abdomen. Examination of the urine revealed large quantities of albumin, with a few casts. The blood chemistry showed: urea nitrogen, 30.8 mg. per hundred cubic centimeters of blood, and cholesterol 0.366 per cent. Examination of the blood showed: leukocytes, 10,000; polymorphonuclears, 51 per cent; eosinophils, 5 per cent, and lymphocytes, 34 per cent. The blood pressure was 145 systolic and 100 diastolic. This was the first time, since our observations began, that there was an increase in the nitrogenous constituents of the blood and in the blood pressure.

On December 22, the patient's weight was 75 pounds (34 Kg.). The blood pressure was 114 systolic and 88 diastolic. The blood chemistry showed: non-protein nitrogen, 50 mg. per hundred cubic centimeters of blood, and cholesterol, 0.228 per cent.

On December 26, when discharged, the patient weighed 72 pounds (32.7 Kg.) and had no visible edema.

Until two weeks before the fourth admission, on July 24, 1924, there was no visible edema. Then the patient again had general anasarca. Two days previously, he complained of abdominal pain. Physical examination showed the patient to be markedly edematous and acutely ill. There was no tenderness over the mastoid or the paranasal sinuses. The lungs and heart were normal. Tenderness was found over the entire abdomen. The blood culture showed a pneumococcus type III. The leukocytes numbered 12,000; the polymorphonuclears, 75 per cent. The temperature was 103 F.

By the next day, all tenderness over the abdomen had disappeared. Two days later, results of the blood culture proved negative. The temperature was still high, and there was a red and tender area in the lower lumbar region.

On July 29, an erysipeloid-like lesion appeared in the lumbar region. The skin was red and exquisitely tender, but the edges of the lesion were not raised.

On August 1, the lesion was improved, but another erythematous patch had appeared on the right leg. The temperature was still elevated. The patient was voiding well. The blood pressure was 124 systolic and 80 diastolic. The next day, the temperature was slightly lower. The erythematous area over the back was smaller but still tender. The redness over the leg was gone.

By August 10, the temperature was still fluctuating from day to day. The blood chemistry showed: urea nitrogen, 30.8 mg. per hundred cubic centimeters of blood, and cholesterol, 0.26 per cent. The patient had lost 6 pounds (2.7 Kg.). The erythematous area in the lumbar region, which was still tender but fluctuated, was incised and drained; the pus contained a pneumococcus type IV. Soon after drainage, the temperature returned to normal and remained there.

When seen on August 29, the child had been placed on a diet containing 20 per cent protein and had lost 22 pounds (10 Kg.). No medication was given. The urine contained considerable albumin and many casts. The blood chemistry revealed: urea nitrogen, 14 mg. per hundred cubic centimeters of blood, and cholesterol, 0.42 per cent.

On September 26, the cholesterol content of the blood was 0.218 per cent; the general condition was about the same.

On November 14, a tonsillectomy was performed.

On November 28, the albumin was less marked. The blood pressure was 100 systolic and 80 diastolic. When discharged, the patient weighed 71 pounds (32.2 Kg.).

On May 12, 1925, the patient was admitted for the fifth time. He had had generalized anasarca since his last discharge. He had been placed on a mixed diet. Two days before admission he had a chilly sensation and edema. He was now acutely ill and his temperature was elevated. The heart and lungs were normal. The abdomen contained fluid but was not tender. On the inner surface of the left thigh there was a small erythematous area which was not tender.

On May 13, the temperature was 103 F. There was no abdominal tenderness, but the erythematous area had extended to the abdomen. It covered the whole thigh and extended upward almost to the umbilicus. The urine contained albumin. The blood chemistry yielded normal results. The cholesterol was 0.344 per cent. The blood culture disclosed pneumococcus type IV.

On May 15, the child died suddenly owing to hemorrhage from the mouth.

Autopsy.—The child was fairly well developed and well nourished, with moderate anasarca, the edema being most marked in the lower extremities, lower part of the abdomen and penis.

The chest was symmetrical, showing no deformities. The pleural cavities were each filled with about 200 cc. of clear yellowish fluid. Together the lungs weighed 560 Gm. They were adherent at both bases, the adhesions being most marked at the peripheral portions of the lower lobe. The parietal pleura over the diaphragm was deeply injected with enlarged venules. There was no fibrinous exudate. The lungs were fairly well aerated. Patchy infiltration was most marked in the upper lobe of the left lung and at the base of both lungs. On section, the lung was red, moderately congested and infiltrated in patches, though the line of demarcation between apparently healthy and infiltrated lung was not marked. The left upper lobe, on section, was a somewhat darker red than the remainder, but its consistency was the same. The lungs throughout were fairly firm, and were not readily friable. The bronchi were normal throughout, except at the left

upper lobe, where there was a deeper red mucoid fluid in the bronchi. No bleeding point could be found leading into it. The vessels and lymph nodes were normal.

A small piece of thyroid tissue about 3 cm. in diameter appeared grossly normal.

The heart weighed 200 Gm. The pericardium was smooth and glistening, containing about 40 cc. of clear yellowish fluid. The heart was practically normal in size, shape and position. The myocardium was firm, and the thickness of the musculature was in normal proportion to the size of the heart. The mitral valve showed a slight amount of thickening at the edges just above the insertion of the chordae tendineae. The thickened portion was brighter red than the adjoining endocardium. The other valves and endocardium were normal. The aorta was elastic and normal in its dimensions. The coronary arteries were normal.

The abdomen was moderately distended with fluid. The panniculus adiposus was fairly well preserved, and about 2 cm. in thickness. The peritoneal cavity contained about 1 liter of turbid greenish-yellow, thin fluid. The omentum was long, ragged and moderately adherent at the left upper quadrant to loops of intestine. The intestinal loops were thickly adherent in the region of the right upper quadrant. The adhesions appeared to be old, but could be cut through without injury to the intestinal wall. No fibrinous exudate was present. There was a slight degree of perisplenitis and perihepatitis.

The liver weighed 134 Gm. There was a slight amount of thickening in patchy areas of Glisson's capsule. The liver on section was brownish yellow. The lobules of the liver could barely be seen. The parenchyma was normal.

The spleen weighed 120 Gm. The capsule was slightly thickened but regular. On section, the spleen was fairly firm and dark red. The malpighian follicles were visible.

The suprarenal glands and the pancreas were normal.

The kidneys weighed 320 Gm. and were about twice the size usually found in a body of this size. The surface was regular. The capsule stripped readily, revealing a finely granular surface, with moderately dilated venules giving it the appearance of fine dark red lines running between whitish parenchyma. On section, the cortex was about 0.5 to 0.7 cm. in diameter, paler than usual and slightly granular. The whitish granular substance continuous with the cortex dipped down between the pyramidal portions to the pelves. The medullary parts were well marked, and grossly normal. The blood vessels, pelves and ureters were grossly normal. The bladder was normal.

The esophagus, stomach and intestines were normal, except for the aforementioned adhesions of the loops at the hepatic flexure.

A few vestigial pieces of thymus tissue, from about 0.5 to 1 cm. in diameter, were embedded in the pericardial connective tissue and fat. These were apparently normal.

Microscopic Examination.—The thymus was in a regressive stage. Numerous Hassel's corpuscles were present, some of which had undergone calcification. The thyroid was normal. There was bulbous thickening of the mitral valve. No bacteria were visible with a special stain. Congestion and edema were found in the lungs. In a few areas there was marked peribronchial thickening. The liver and pancreas were normal.

Examination of the kidneys showed a diffuse tubular degeneration and a moderate dilatation of the lumina of the tubules. In numerous places these degenerated cells had undergone calcification. In one or two areas, Bowman's capsule was definitely thickened and the glomerular cusps were adherent. There were, likewise, numerous linear areas of round cell infiltration in the cortex.

Sudan III stained many of the descending Henle loops; some primary convoluted tubules showed amorphous masses of calcium plugging the lumina. There was a rich and abundant deposit of neutral fat in many of the convoluted tubules. Masses of fat were contained in the lumina and others in wandering cells. Fatty deposition was not diffusely distributed but was rather patchy. The epithelium of the tubules was completely necrotic and infiltrated by droplets of neutral fat in some areas. In areas such as these, interstitial infiltration was especially marked.

CASE 7.—A boy, aged 4 years, admitted on May 27, 1925, with an unimportant family history, had had scarlet fever one year before. Five weeks before admission, the mother noticed that the child's face was swollen. For the last few days he had had a slight cough.

Examination.—On admission the patient appeared to be acutely ill, showing a moderate general anasarca. The teeth were in poor condition, the tonsils small and the lungs and heart normal. The abdomen was distended but no fluid was noted. The blood pressure was 80 systolic and 60 diastolic. Examination of the urine showed large quantities of albumin. Microscopically, a few hyaline and granular casts and a moderate number of red and white blood cells were seen. The blood chemistry revealed: urea nitrogen, 12.6 mg. per hundred cubic centimeters of blood, and cholesterol, 0.148 per cent. The child was placed on a balanced diet with 1,000 cc. of fluid. His weight was 46 pounds (20.8 Kg.).

After admission, the edema increased. On June 23, the blood chemistry showed: urea nitrogen, 21 mg. per hundred cubic centimeters of blood, and cholesterol, 0.29 per cent. The total serum protein was 4.1 per cent, the globulin being 2.4 per cent. Abdominal paracentesis was performed and 2,000 cc. of fluid withdrawn; culture of the fluid yielded negative results.

On July 15, there was abdominal pain, a temperature of 104 F. and severe diarrhea.

On July 17, there was an erysipeloid eruption in the region of the right groin. The blood culture was positive and showed pneumococcus type IV.

On July 20, the skin lesion in the right groin had disappeared, but another spot appeared over the left thigh and ankle.

On July 26, a blood culture gave negative results. The patient's general condition had improved; the edema was markedly less. The patient had lost 19 pounds (8.6 Kg.). The urine contained albumin and a few casts. The leukocyte count was usually about 20,000, with 60 per cent polymorphonuclears.

On August 6, the patient was discharged, with little visible edema; the cholesterol content of the blood was 0.17 per cent.

On Jan. 4, 1926, he was readmitted. He had done fairly well for a few months and then had contracted varicella, following which the edema had returned. As soon as the patient had recovered from the infection the edema disappeared, only to return again. His physical condition, except for increased edema, was no different than on discharge. The blood pressure was normal. The urine contained large amounts of albumin and a few casts and white cells. The blood chemistry showed: urea nitrogen, 21 mg. per hundred cubic centimeters of blood, and cholesterol, 0.5 per cent.

On January 12, there was abdominal pain and a temperature of 101 F. The abdomen was distended and tender. A blood culture gave negative results. Roentgen examination showed the paranasal sinuses to be normal.

On January 19, the urea nitrogen amounted to 14.6 mg. per hundred cubic centimeters of blood, and the cholesterol, 0.343 per cent.

On January 29, abdominal paracentesis was performed; 500 cc. of cloudy fluid was obtained which showed gram-positive diplococci on smear; culture of the fluid, however, gave negative results.

On February 24, a high temperature developed which continued for three days. The blood culture, however, gave negative results.

On March 7, an eruption was noted on the face and the upper and lower extremities. It looked like urticaria and was present at various intervals for many months. Skin sensitization tests gave negative results. The patient was sent to the Convalescent Home.

On July 3, the patient was readmitted after having been in poor condition in the Convalescent Home. He showed general anasarca, but no other unusual symptoms.

On July 27, examination showed that he had lost weight but that his general condition was better.

On August 29, he was discharged. The edema had disappeared, and the cholesterol content of the blood was 0.42 per cent.

On October 21, the patient was admitted for the fourth time with the report that he had been in good condition until the week before, when a cold developed. Four days before, the face became swollen. Twelve hours before admission, he had sudden abdominal pain. Physical examination showed that the patient was acutely ill. The abdomen was distended, tender and rigid. The heart and lungs were normal. Blood culture showed pneumococcus type IV. The temperature was 103 F. Examination of the blood revealed: leukocytes, 41,000, and polymorphonuclears, 86 per cent.

On October 25, the blood culture again showed pneumococcus type IV. The temperature was 103 F., but the abdomen was less tender. An erysipeloid rash was present on both cheeks.

On October 27, the blood culture gave negative results, as did the nasal examination. The lesions on the cheeks had disappeared. The blood chemistry showed: urea nitrogen, 14 mg. per hundred cubic centimeters of blood, and cholesterol, 0.276 per cent. The edema was disappearing.

On November 29, the papular urticaria previously described was again present. The blood pressure was normal.

On December 27, a tonsillectomy was performed with no reaction. The patient was discharged with little edema and normal blood pressure. The cholesterol content was 0.39 per cent and the serum protein, 3.95 per cent.

On September 9, the patient was admitted for the fifth time. He had been in fairly good condition until six weeks before, when he had mumps. The day before admission he had pain in the left leg. Physical examination did not disclose acute illness. The nose and throat were normal, as were the lungs and heart. The abdomen was slightly enlarged, and the liver and spleen were slightly palpable. The extremities showed little edema. Examination of the blood showed: hemoglobin content, 60 per cent; red cells, 4,300,000; white cells, 8,400; polymorphonuclears, 44 per cent, and lymphocytes, 54 per cent. Chemical examination of the blood revealed: urea nitrogen, 11 mg. per hundred cubic centimeters of blood; cholesterol, 0.39 per cent; total protein, 3 per cent; total globulin, 1.2 per cent, and total albumin, 1.8 per cent. The urine contained a large amount of albumin, and had high specific gravity. The concentration test gave normal results. The patient was in the hospital for two weeks; during this time he lost about 5 pounds (2.3 Kg.). He was discharged, and referred to the follow-up clinic.

On September 30, the patient was readmitted, as the edema was increasing. The general condition had not changed. Clubbing of the fingers and toes was

fairly well marked. The blood pressure was 112 systolic and 76 diastolic. Examination of the urine showed albumin 3 plus. Microscopically, an occasional hyaline cast was observed. The blood chemistry showed: urea nitrogen, 13 mg. per hundred cubic centimeters of blood, and cholesterol, 0.46 per cent. There was no fever, and the results of a blood culture were negative. Peritoneal puncture showed the acitic fluid to be sterile; no organisms were seen on a smear. Examination of the nose and throat by Dr. Yankauer disclosed no disease of the paranasal sinus. Roentgen examination showed normal sinuses. The basal metabolism was normal, although 6 grains (0.4 Gm.) of thyroid had been given for two weeks. During this time the patient lost 5 pounds (2.3 Kg.).

On November 23, the temperature was 100.6 F. The blood culture gave negative results.

On December 11, the temperature was 101 F. for a few hours, and results of the blood culture were negative.

On December 27, the temperature was 102 F., and the patient vomited all food taken. There was slight abdominal pain. The blood culture showed hemolytic streptococcus, 1 colony per cubic centimeter. The blood cholesterol was 0.554 per cent. Two days later the culture again yielded hemolytic streptococci.

On December 30, the temperature continued to be elevated (from 103 to 105 F.). There was abdominal tenderness, perhaps more marked in the right lower quadrant. The lungs and pharynx were normal.

On December 31, the vomiting ceased. The temperature was normal, and the abdominal pain had disappeared.

On Jan. 19, 1928, the cholesterol content was 0.346 per cent; total protein, 4.5 per cent; total globulin, 2.19 per cent, and total albumin, 1.6 per cent.

On April 23, the patient was admitted for the seventh time. He had been well for the previous three months, except for a moderate amount of edema of the legs and the face. For seven days preceding admission, he had had a coryza. Six hours before admission, he awakened from sleep complaining of severe abdominal pain; he vomited and had a chill which lasted about five minutes. On examination, the patient proved to be acutely ill and apparently was in great pain. The pharynx was pale, and the abdomen greatly distended and tender throughout. A peritoneal puncture revealed turbid fluid, which yielded pneumococcus type IV. Roentgenograms of the chest showed no infiltration of the lungs. Roentgenograms of the nasal sinuses showed some clouding of the right antrum.

On April 26, the child's condition became worse, and he died.

Autopsy.—Large and edematous kidneys were revealed. A large amount of double refractory fat was seen in the cortex. Microscopically, many sections showed no inflammatory change of glomeruli or interstitial tissue. The tubules were the same as those reported in other cases.

COMMENT

The clinical picture in cases with a positive blood culture seems to be of two types: In one, the predominating symptoms are abdominal; in the other, rhinopharyngeal. In the first type, the onset usually occurs during the stage of generalized edema, and is associated with severe abdominal pain, nausea and vomiting. The pain is fairly continuous and will keep the child awake at night. There may or may not be much increase in temperature. On examination, the child is

found to be acutely ill, and the abdomen markedly distended and rigid, with generalized and rebound tenderness. The acute pain and tenderness lasts for about twenty-four hours and gradually subsides, becoming almost negligible in three or four days. The temperature, if elevated, also returns to normal within three or four days. There may be only a slight increase in temperature during the entire attack. These attacks may be repeated several times throughout the course of the disease. The edema is usually uninfluenced by the attack. This clinical picture was seen in four cases and occurred in three boys and one girl (cases 5, 6, 7 and 9).

The rhinopharyngeal type of clinical picture may appear at any time in the course of the illness. There is an inflammation of the rhinopharynx, or perhaps some other manifestation of an infection of the upper respiratory tract. On inspection, the child appears acutely ill; the rhinopharynx may or may not show an exudate. An exudate is often seen on the uvula. The temperature is high, and in a few days the picture may be clouded by signs of a pneumonia or a peritonitis. This type of illness was observed in two of the cases (cases 1 and 3). Edema was present during the period of general bacterial invasion.

Blood cultures were taken daily when the temperature was at all elevated. When taken on the first day of fever the cultures gave positive results on four occasions, and negative on seven. In two cases, blood cultures taken on the second day of fever gave positive results; and in four cases blood cultures taken on the third day of fever gave positive results. After the third day the cultures yielded negative results. In one case the blood culture gave positive results even though the temperature was below 100 F. In another case a hemolytic streptococcus was obtained once and a pneumococcus type IV on three other occasions. In five cases the pneumococcus type IV was obtained; in one case pneumococcus type III, and in two cases *Streptococcus hemolyticus* (table 1). Thus it would appear that positive results are obtained from blood cultures only on the first three days of fever.

The bacteria grow equally well on solid and fluid mediums. When recovered from the blood, the organisms are usually not found in large numbers except in moribund patients.

Skin manifestations are not uncommon in this disease. They are present with or without fever and with or without positive results from blood cultures. An erysipeloid lesion is most often noted. It is most frequently seen in the lumbar region and on the lower extremities; rarely on the face. It starts as a small reddish area which spreads peripherally. It is not as red as the true lesion of erysipelas nor is the margin raised. The duration of the lesion before fading is from three to five days, after which there is scaling of the skin at the site of the lesion. This type of lesion was seen in four cases (cases

4, 6, 7 and 8). Sometimes the lesion persists and may break down, forming an abscess in the skin. This occurred in case 6; a pneumococcus was found in the pus obtained.

Other skin lesions appearing during the course of the nephrosis were various types of urticarial eruptions and prurigo-like lesions. These lesions occurred in three cases (cases 2, 7 and 8). They have been described by Goldenberg and Rosen.[2] Under treatment and with improvement of the underlying conditions, the eruption became milder and the itching less intense. Similar lesions are occasionally seen in leukemia and Hodgkin's disease.

SUMMARY

Nine cases of clinically typical lipoid nephrosis in children were studied. Bacteria were repeatedly found in the blood stream, in the ascitic fluid and in lesions of the skin. The significance of this fact is left for future study.

110 East Ninetieth Street.

55 East Eighty-Sixth Street.

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Case Reports

GAUCHER'S DISEASE

A REVIEW OF THE LITERATURE AND REPORT OF A CASE DIAGNOSED FROM SECTION OF AN INGUINAL LYMPH GLAND *

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In 1882 Ernest Gaucher [1] described a form of splenic anemia which he termed "primary idiopathic hypertrophy of the spleen," and which today bears his name. It was not until thirteen years later that Collier [2] in England, and Picou and Ramond [3] in France, described the next cases. In 1900, Bovaird [4] reported the first American case. In 1904, Brill and Mandlebaum [5] added the next case to the literature, in which they described for the first time the occurrence of the large characteristic cells in the bone-marrow, and also added much to the knowledge of the pathology of this disease. Schlagenhaufer,[6] in 1907, reported the first case in the German literature. Since then, cases have been reported at regular intervals and with increased frequency. Mandlebaum,[7] in 1919, stated that up to date there were twenty-one authentic cases on record. Ludwig Pick,[8] in 1926, collected thirty-nine cases to date, five of which

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1. Gaucher, E.: De l'epithéliome primitif de la rate: hypertrophie iodopathique de la rate sans leucémie, Thèse de Paris, 1882.

2. Collier, William: A Case of Enlarged Spleen in a Child Aged Six, Tr. Path. Soc. Lond. **46**:148, 1895.

3. Picou, R., and Ramond, F.: Splénomegalie primitive, épithéliome primitif de la rate, Arch. de méd. exper. et d'anat. path. **8**:168, 1896.

4. Bovaird, David: Primary Splenomegaly, Endothelial Hyperplasia of the Spleen: Two Cases in Children; Autopsy and Morphological Examination in One, Am. J. M. Sc. **120**:377, 1900.

5. Brill, N. E.; Mandlebaum, F. S., and Libman, E.: A Case of "Splénomégalie Primitif" with Involvement of the Haemopoietic Organs, Proc. New York Path. Soc. **4**:143, 1904.

6. Schlagenhaufer: Ueber meist familiär vorkommende, histologisch characteristiche Splenomegalien, Virchows Arch. f. path. Anat. **187**:125, 1907.

7. Mandlebaum, F. S.: Two Cases of Gaucher's Disease in Adults: A Study of the Histopathology, Biology and Chemical Findings, Am. J. M. Sc. **157**:366, 1919.

8. Pick, Ludwig: Der Morbus Gaucher und die ihm ähnlichen Erkrankungen, Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.

were seen and reported by him personally. Twenty-two of the thirty-nine cases have been reported during the last two years. It is to this author that we owe much of our present knowledge and conception of this disease and differential diagnosis for similar conditions. Cushing and Stout,[9] in the same year, in this country, collected fifty cases. We have reviewed the literature to date and report our case, making the total eighty-nine.

Since this condition was first described, many theories have been advanced as to its pathogenesis. The original neoplastic conception of the nature of the cells was replaced by that of hyperplasia, one tracing the origin to endothelial lining of the venous spaces [2] and the other to the reticular tissue of the pulp.[10] Marchand [11] considered the process due to the deposition of some foreign substance in the cells. Mandlebaum and Downey [12] proved conclusively the origin of the Gaucher cells from the reticulum of the lymphatic-hematopoietic system, and they were also led to believe that the disease was fundamentally some disturbance in lipoid metabolism. Epstein [13] and Lieb [14] showed that this substance is a sphingogalactoside called kerasin, soluble in warm alcohol and insoluble in ether, formed by the linkage of lignoceric acid, sphingosin and d-galactose. These observations were confirmed by several investigators. From our present knowledge of the microscopic changes and clinical manifestations of this condition, the condition may be defined as a familial, congenital and nonhereditary disease probably due to a disorder in the lipoid metabolism characterized by the deposition of complex lipoid mixtures in the reticulum and adventitial cell of the hematopoietic organs and clinically manifested by splenomegaly, hepatomegaly, moderate generalized lymphadenopathy, pigmentation of the skin, pingueculae, hemorrhagic diathesis, changes in the bone, hypochromatic anemia, leukopenia and thrombocytopenia. The course is usually chronic, often lasting twenty years or longer, exacerbations occurring in the course of complicating infections.

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9. Cushing, E. H., and Stout, A. P.: Gaucher's Disease, Arch. Surg. **12**:539 (Feb.) 1926.

10. Risel, W.: Ueber die grosszellige Splenomegalie (Typus Gaucher) und über das Endotheliale Sarkom der Milz, Beitr. z. path. Anat. u. z. allg. Path. **46**:241, 1909. De Jong, R., and van Heukelom, J. Siegenbeek: Beitrag zur Kenntnis der grosszelligen Splenomegalie (Typus Gaucher), Beitr. z. path. anat. u. z. allg. Path. **18**:598, 1910. Schlagenhaufer (footnote 6).

11. Marchand: Ueber sogenannte idiopathische Splenomegalie (Typus Gaucher), München. med. Wchnschr. **54**:1102, 1907.

12. Mandlebaum, F. S., and Downey, H.: The Histopathology and Biology of Gaucher's Disease (Large-Cell Splenomegaly), Folia haemat. **20**:139, 1916.

13. Epstein, E.: Beitrag. zur Chemie der Gaucherschen Krankheit, Biochem. Ztschr. **145**:398, 1924.

14. Lieb, Hans: Cerebrosidspeicherung bei Splenomegaly, Typus Gaucher, Ztschr. f. phys. Chem. **140**:305, 1924.

Splenomegaly, in infancy and childhood, occurs rather frequently. The underlying pathologic process is often obscure and undiagnosed unless the patient reaches the autopsy table. Because of the many common conditions associated with splenomegaly at this period of life, the diagnosis is much more difficult than in adults. The rarer forms of splenic enlargements are frequently overlooked.

The symptomatology of Gaucher's disease as it presents itself in infancy and childhood is somewhat different from that in the adult. Approximately one third of the cases of this condition as reported in the literature occurred in children under the age of 14; ten have occurred in children under 1 year of age. We therefore feel that this form of splenic anemia is of the most particular interest to the pediatrician.

ETIOLOGY

The disease is undoubtedly of familial incidence. Collier [2] first reported its occurrence in more than one member of a family. Pick [8] stated that there was a familial history in more than one third of the cases reported up to 1926. In the eighty-nine cases cited, thirty, or approximately one-third, are of familial character. In no series of children has either of the parents suffered from the disease, nor has it been transmitted from any adult to a child. Four cases of this disease have been reported in the same family. The condition is somewhat more common in the female; 55 per cent of the cases occurred in this sex.

Reuben,[15] in 1914, collected fourteen cases in children which dated from the time of Gaucher up to date. Oberling and Woringer [16] stated that one third of the forty cases reviewed by them occurred in patients under 16 years of age. These same authors cited four cases in infants under 1 year of age, which together with those reported by Rusca,[17] Gerstl,[18] Kohn,[19] Nauwerck and Pick,[20] and Reber [21] bring the number of cases occurring in infants under 1 year to nine. In the eighty-nine cases collected by us, fifteen, or approximately 16 per cent, occurred in patients at the age of 1 year or under; twenty-eight, or approximately 30 per cent, under 5; thirty-eight, or approximately 40 per cent, under

15. Reuben, M. S.: Gaucher's Disease, Arch. Pediat. **41**:456 (July) 1924.

16. Oberling and Woringer: La maladie de Gaucher chez le nourrisson, Rev. franç. de pédiat. **3**:475, 1927.

17. Rusca, C. L.: Sur morbo del Gaucher, Haematologica, Arch. ital. di ematolog. e sierol., Napoli **2**:441, 1921.

18. Gerstl and Kraus: Zur Kenntnis der Splenomegalie Gaucher insbesondere der Histogenese der grosszelligen Wucherung, Ztschr. f. ang. Anat. **7**:186, 1921.

19. Kohn, reported by Oberlin and Woringer: Rev. franç. de pédiat. **3**:475, 1927.

20. Nauwerck, cited by Pick: Med. Klin. **18**:1408, 1922.

21. Reber, M.: Zur Splenomegalie Gaucher im Säuglinsalter, Jahrb. f. Kinderh. **3**:277, 1924.

12 years; fifty-two, or approximately 51 per cent, under 25 years. The greatest number of cases occurred in patients under 5 and between the ages of 25 and 35. The youngest patient on record was reported by Siegmund [22] with the onset at 1 week of age. Bruce [23] reported the case of a patient with the onset of disease at 43. The average age of onset in these eighty-nine cases is 11 years. This disease no doubt is congenital and may manifest itself at any age.

Schlagenhaufer [6] and Ewing [24] thought that tuberculosis might be an etiologic factor, as evidenced by the frequency of tuberculous condition at autopsy. Spackman and Mackie [25] stated that the disease is common in India. They are alone in their observation.

PATHOLOGY

Pick [26] has excellently described the pathologic process of this disease as it is known today. It is chiefly a disturbance of lipoid metabolism with the production of an abnormal substance which is stored by histiocytes of reticulo-endothelial origin, giving rise to the typical Gaucher cell which is found in all tissues in which reticulo-endothelium is present, involving chiefly the spleen, lymph glands, liver and bone (fig. 1 and accompanying pathologic report for the description of the typical cell).

CLINICAL FEATURES

The onset is usually insidious. The discovery of an enlarged spleen is often an incidental condition during the course of a routine examination. In many instances it is difficult to say just when the disease actually began. In infants the onset is more acute, with neurologic symptoms often predominating. There is usually no sign of this illness at birth. The children are well developed and nourished. Only in the case of Reber [21] was the infant debilitated, and in that of Gerstl and Kraus,[18] it was premature, being born at eight months. In Kohn's [19] patient an enlarged spleen was found during the first week of life, leading him to believe that the condition might be congenital. Oberling and Woringer [16] stated that the outstanding symptoms in infants are retardation in physical development, increase of weight due to the splenomegaly, apathy, rigid neck, hypertonicity, opisthotonos and emaciation.

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22. Siegmund: Lipoid Zellenhyperplasie der Milz und Splenomegalie Gaucher, Verhandl. d. deutsch. path. Gesellsch. **18**:59, 1921.

23. Bruce, H. A.: A Case of Large, Celled Splenomegaly (Gaucher Type), Tr. Am. Surg. A. **38**:288, 1915.

24. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922, p. 313.

25. Spackman and Mackie: Indian Gaz. **60**:69, 1925.

26. Pick, Ludwig: Zur pathologischen Anatomie des Morbus Gaucher, Med. Klin. **18**:1408 (Nov.) 1922.

The symptoms at onset in the adult usually manifest themselves in abdominal pains or pains of the bone. Not infrequently, a purpuric diathesis brings the patient to the physician.

Splenomegaly has been a constant symptom and is usually the predominating feature in the disease. The growth of the spleen is slow and progressive; at times it may assume tremendous proportions (one sixth of the body weight). Brill, Mandlebaum and Libman [27] reported a case in which the spleen weighed 8,100 Gm. The organ may approach the left iliac crest and extend beyond the midline. The notch is usually palpable, the edge firm and sharp. Tenderness may be present. The abdominal symptoms are due either to the perisplenitis and hepatitis or to the dragging sensation of weight of the splenic tumor. The abdominal pain is most frequent in the left quadrants.

The peripheral lymph glands are only moderately enlarged if at all. In eighteen of the collected cases, there was a definite history of lymphadenopathy. The axillary glands were most frequently enlarged. Nine cases showed inguinal adenopathy. The glands of the neck were least involved. Generalized peripheral involvement is not common. These glands are usually the size of a bean and are not tender. Visceral glandular enlargement is common. The size depends on the extent of the involvement. The perisplenic, mesenteric and retroperitoneal glands were found to be most frequently enlarged. A few cases showed tracheobronchial, perihepatic and pancreatic involvement.

There is moderate enlargement of the liver. Often it is barely palpable. A few cases showed no hypertrophy. Sometimes it may extend below the umbilicus to the iliac crest and past the midline. Its edge is firm, sharp and smooth. This hepatic enlargement is usually secondary to the splenomegaly. Perihepatitis is present which may often be a cause of abdominal distress.

When discoloration of the skin is present, it is due to a hematochromatic pigmentation. This pigmentation is most frequently seen in the exposed parts, the face and extremities, the color varying from brownish yellow to bronze; it is probably due to a deposition of a lipochrome and not bile pigments.[8] Forty-five per cent of the cases showed this pigmentation. Warren [28] stated that it was present in 75 per cent of the cases.

The brown, wedge-shaped discoloration in the subconjunctivae, the pingueculae, is not as frequent as previously supposed. Although Brill and Mandlebaum [27] maintained that it is always present, it has been mentioned in only fourteen cases reported. Graham and Blacklock [29]

27. Brill, Mandlebaum, and Libman: Gaucher's Disease, Am. J. M. Sc. **137**:849, 1909.

28. Warren, L.: Warthin Ann., 1927, p. 535.

29. Graham, S., and Blacklock, J. W. S.: Gaucher's Disease, a Clinical and Pathological Study, Arch. Dis. Childhood **2**:267, 1927.

did not find them in their series. Seven of the eleven cases recently reported by Welt and her co-workers [30] showed these pingueculae.

The hemorrhagic diathesis occurs frequently. Forty-seven of the reported cases presented this symptom. It was manifested as epistaxis in twenty-four, bleeding from the gums in fourteen, purpuric spots in ten, petechias in six, hemoptysis in five, and menorrhagia in six. One, two, or a combination of any of these mentioned may occur in the same patient. In four of five cases reported by Graham and Blacklock [29] there was bleeding from the gums.

Twenty-two cases of this group had symptoms referable to the skeletal structure. The femur, vertebrae, the hip, sternum, tibia and fibulae were the bones most commonly involved. Pains in leg, knee or hip, shortening of one limb or gibbus formation were the common symptoms. Pathologic fractures were less frequent. Kraus [18] observed in two cases the lack of general development of the skeletal structure as well as mental inferiority. Six of the cases recently reported by Sara Welt and her co-workers [30] showed definite and variable changes of the bone, these being manifested roentgenologically in the long bones in the form of mottling, rarefaction, at times condensation and expansion of the bone, a disappearance of the demarcation between the marrow and the cortex and a marked thinning, but usually not a direct destruction, of the cortex. They stated that a diffuse expansion of the lower third of the femurs, especially toward the internal condyle, obliterating the normal contour, is an early roentgenographic sign. The mottled, worm-eaten appearance is probable evidence of an advanced state of bone involvement.

In children, nervous symptoms are frequently superimposed on the visceral lesion, and cachexia is much more rapid. Opisthotonos, spasticity, strabismus, rigidity of the neck and pathologic reflexes were present in the four cases reported by Oberling and Woringer.[16] This syndrome was described as a "progressive decortication."

The blood usually shows a hypochromatic anemia of 3,000,000 or 4,000,000 red cells with a leukopenia. It is interesting to note that following splenectomy a leukocytosis usually appears. Thrombopenia was observed in those cases in which a platelet count was made. In our case the determination of the blood lipoids showed a slight decrease in the phosphatids, a marked decrease in cholesterol and normal total of fatty acids (table 1).

The course is usually chronic. Exacerbations occur in the course of other infections, and remissions follow. Death is usually due to some intercurrent disease. In infants the course is much more rapid, the

30. Welt, Sara; Rosenthal, Nathan, and Oppenheimer, B. S.: Gaucher's Splenomegaly: With Especial Reference to Skeleton Changes, J. A. M. A. **92**:637 (Feb. 23) 1929.

duration being approximately six months. Splenectomy does not effect a cure, and in some cases affords only a symptomatic relief. In children the condition often becomes aggravated.

REPORT OF CASE

History.—A colored boy, aged 17 months, entered the Cook County Hospital pediatric department, on the service of Dr. Julius H. Hess, on Jan. 23, 1929, with a diagnosis of leukemia and meningitis. The history was obtained from the grand-

Fig. 1.—Gaucher's cells in lymph gland; fixed with 10 per cent formaldehyde hemalum stain; magnification × 625.

mother. The complaints were "cold" for two weeks, swelling of the left side of the neck for four days, purulent discharge from the left ear for one day, swelling of the abdomen for two weeks, restlessness for two weeks and stiffness of the entire body for the past four days.

The patient was apparently well until two weeks prior to his entrance to the hospital, when he contracted a "cold" which manifested itself by sneezing and a mild cough. Progressive abdominal swelling was soon noticed. Four days before admission, the child became restless and cried continually; he became rigid and markedly spastic, assuming the position of opisthotonos. The left side of the neck became swollen and tender to touch. On the day of entrance to the hospital, a discharge was noticed from the left ear.

The patient was a full-term infant of the second pregnancy. The birth history was normal. The child weighed 10 pounds (4.5 Kg.) at birth. No asphyxia or cyanosis was present. He was breast fed until 10 months of age, and was then put on a variable formula of cow's milk. Administration of cod liver oil was instituted at 6 months and orange juice given at variable intervals. The development of the child was somewhat retarded. The first tooth appeared at 8 months; he sat up at 7 months and had not walked or talked.

The mother was a secundipara with no history of miscarriages, and was apparently in good health. The father was living and well. There was no history of

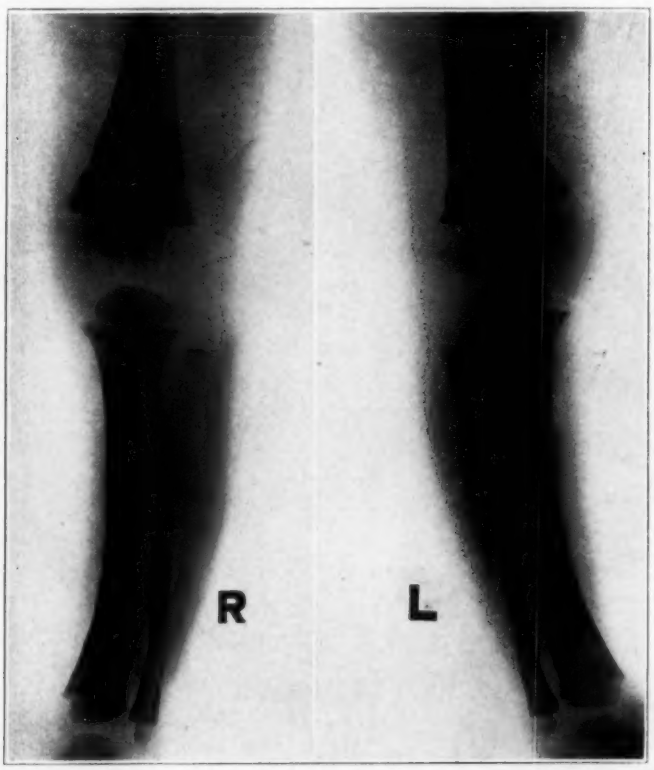

Fig. 2.—Lower extremities.

tuberculosis or carcinoma. A brother, aged 3, was apparently in good health. No history of abdominal enlargement could be obtained in any of the immediate family. The medical and surgical history of this child was negative.

Examination.—Physical examination showed a colored boy, aged 17 months, who was fairly well nourished, weighing 23 pounds (10.4 Kg.). The temperature was 102 F. (rectal), the pulse rate 120 and respiratory rate 30. The child appeared to be acutely ill, was extremely restless and irritable and assumed a position of opisthotonos with moderate amount of spasticity. The head was tilted to the right and retracted. The anterior fontanel was patent and not bulging. The pupils were equal and regular and reacted to light. The sclerae were white and not pigmented; wedge-shaped areas were not seen. There was a slight mucopurulent

discharge from the nose. A diffuse purulent discharge was present, excoriating the left ear. The right ear drum was reddened but not bulging. The mouth was open, revealing a dry coated tongue which was not enlarged or protruding. The tonsils were enlarged, cryptic and injected. The pharynx was also somewhat injected and contained a great deal of sticky mucus. Passive flexion of the head was difficult; there was no Brudzinski sign.

The neck presented cervical and submaxillary glands enlarged to the size of a walnut on the left side. They were indurated, nonfluctuant, fairly well circumscribed and somewhat tender. The right cervical glands were enlarged to the size of a bean, but were not tender. The posterior cervical, as well as the submental glands, were also enlarged.

The chest was symmetrical. There was some enlargement of the costochondral junction, with some flaring of the ribs. The resonance of the lungs was normal, with a few scattered râles in the base of the right lung. The borders of the heart were within normal limits, and the tones were clear and regular. There were no murmurs. The axillary lymph glands were definitely enlarged on both sides.

The abdomen was markedly distended and tender, with no evidence of fluid, the left side being somewhat more prominent than the right. The liver was greatly enlarged, extending down to the umbilicus and two fingerbreadths to the left of the midline. It was smooth and firm, and its edge was hard. The spleen

TABLE 1.—*Determination of Blood Lipoids per Hundred Cubic Centimeters*

	Normal, Mg.	Niemann-Picks,* Mg.	Gaucher, Mg.
Phosphatides	12- 14	24	9.5
Cholesterol	140-170	231	80
Total fatty acids	290-420	560	349

* Berman, S. L.: Lipoid Histiocytosis, Am. J. Child. Dis. **36**: 102 (July) 1928.

extended beyond the umbilicus, the splenic notch being definitely palpable. A slight umbilical hernia was present. The inguinal lymph glands were enlarged to the size of a bean.

The genitalia were normal.

The extremities showed evidence of rickets. They were hypertonic and somewhat spastic. The reflexes were exaggerated. No pathologic reflexes were elicited.

The skin was soft and had a fairly good turgor. Two mongolian spots were present in the sacral region. The subcutaneous fat was fairly well preserved.

The tuberculin and Wassermann tests were negative. The urine was normal. On spinal puncture the fluid was clear and somewhat increased in pressure, with negative reactions to the globulin test and six cells.

On January 23, the blood count showed: hemoglobin, 70 per cent (Tallqvist); red blood cells, 4,000,000; white blood cells, 26,000; polymorphonuclears, 67 per cent; eosinophils, 3 per cent; lymphocytes, 25 per cent; monocytes, 5 per cent. On January 25, the blood count was: hemoglobin, 70 per cent (Tallqvist); red blood cells, 4,000,000; white blood cells, 16,800; polymorphonuclears, 68 per cent; eosinophils, 2 per cent; lymphocytes, 30 per cent. The blood lipoids were determined and total fatty acids were found to be 349 mg.; phosphatides, 9.5 mg., and cholesterol 80 mg. per hundred cubic centimeters of blood.

On January 27, the hemoglobin showed 6.2 Gm. or 39 per cent hemoglobin (Newcomer). The red cell count was 4,190,000 and the white cell count, 31,350. In the differential (400 cells were counted) there were 16 per cent lymphocytes, 71 per cent polymorphonuclears, 2 per cent transitionals, 0.5 per cent plasma cells, 5

TABLE 2.—*Complete Tabulation of the Cases of Gaucher's Disease up to the Present Time* *

No.	Author	Sex and Age	Age at Onset	Familial	Spleen	Liver	Lymph Nodes	Bones	Hemorrhages	Discoloration of Skin	Eye	Blood: Red Blood Cells	Blood: White Blood Cells	Blood: Hemoglobin, %	Comment
1	Gaucher [1]	Female 32 yr.	7 yr.	.....	4,777 Gm.	3,480 Gm.	.....	Pain	Epistaxis and ecchymoses	+	+	2,281,000	3,627	..	Treated with iron and arsenic; died from pulmonary tuberculosis
2	Collier [2]	Female 6 yr.	2 yr.	Sister died with a large spleen	2,070 Gm.	.....	.....	.....	Epistaxis	..	..	Normal			Died; cause unknown
3	Picou and Ramond: footnote 3; Arch. de méd. expér. et d'anat. path. **8:** 168, 1896	Female 38 yr.	32 yr.	.....	5 cm. below costal margin, 2,800 Gm.	.....	.....	.....	Gums and menorrhagia	+	..	Anemia			Splenectomy; postoperative enlargement of the liver; pain over splenic area prior to operation
4	Bovaird [4]	Female 13 yr.	3 yr.	Sister had bronze skin	6,250 Gm.	2,380 Gm.	Small right inguinal and axillary	.....	.....	+	..	2,800,000	4,000	60	Splenectomy; died 3 hours after operation; pain in upper left quadrant
5	Brill, Mandlebaum and Libman: footnote 5; Am. J. M. Sc. **129:** 491, 1905	Male 34 yr.	19 yr.	Sister	5,280 Gm.	4,800 Gm.	Small axillary	Pain ?	Epistaxis	+	+ ?	4,400,000	5 210	55	Died from hemorrhagic pericarditis with ascites; brother of patient in case 10
6	Schlagenhaufer: footnote 6; Verhandl. d. deutsch. path. Gesellsch. **10:** 77, 1907	Female 43 yr.	5 yr.	Sister had large spleen	3,510 Gm.	3,000 Gm.	Tuberculous glands of the neck	.....	Epistaxis	+	..	4,700,000	1,300	65	Died from tuberculosis
7	Von Herczel: Wien. klin. Wchnschr. **20:** 123, 1907	Female 37 yr.	31 yr.	.....	5 cm. below costal margin, 3,000 Gm.	Palpable	.....	.....	Epistaxis and menorrhagia	+	..	4,200,000	7,000	92	Pain in upper left quadrant; splenectomy; 5 months after operation, liver same size
8	Marchand [11]	Female	.....	.....	5 cm. below costal margin	Palpable	.....	.....	Tendency to hemorrhages	+	..	Unchanged			Twenty years' duration; no clinical history; died from cachexia
9	Risel: footnote 10, first reference	Female 45 yr.	.....	.....	2,720 Gm.	Very much enlarged	Axillary and mesenteric cervical	Sternum and right femur showed flaking of bone	.....	..	..	.....	.....	..	Died from cachexia and calcified pericarditis
10	Brill, Mandelbaum and Libman [27]	Female 37 yr.	21 yr.	Brother	8,100 Gm.	3,900 Gm.	Slight general	Femur marrow showed flaking	Epistaxis	+	+	3,500,000	3,600	35	Died from accident; sister of patient in case 5

11	De Jong and van Heukelom: footnote 10, second reference	Female 12½ yr.	7½ yr.	Brother and sister	1,850 Gm.	.....	.....	.....	Epistaxis	+	..	.....	.....	..	Pain over spleen; splenectomy; 6 months after operation, patient well; liver larger
12	Mandlebaum, F. S.; J. Exper. Med. **16**: 797, 1912	Male 4½ yr.	3½ yr.	Sister	490 Gm.	730 Gm.	Tracheobronchial; mesenteric; retroperitoneal	Femur marrow showed flaked appearance	Epistaxis	+	..	2,200,200	500	35	Splenectomy; died 24 hours after operation
13	Wilson: Surg. Gynec. Obst. **16**: 240, 1913	Female 27 yr.	12 yr.	.....	Spleen below umbilicus, 5,280 Gm.	5 cm. below costal margin	.....	.....	.....	..	..	5,200,000	4,000	80	Splenectomy; died 12 hours after operation
14	Downes, W. A.: Med. Rec. **83**: 697, 1913	Female 28 yr.	15 yr.	.....	Spleen below umbilicus, 1,813 Gm.	Less than 5 cm. below costal margin	.....	Pain	.....	+	+	3,800,000	900	40	Splenectomy; was well until 3 years after operation, liver increased to iliac crest
15	Babes, Aurel and Babes: Compt. rend. Soc. de biol. **75**: 575, 1913	Female 22 yr.	21 yr.	.....	3,020 Gm.	Palpable	.....	.....	.....	.	..	4,800,000	.....	..	Splenectomy
16	Sapegko: Arch. per le sc. med. **37**: 323, 1913	Male 47 yr.	.....	.....	5 cm. below costal margin	.....	.....	.....	.....	..	..	.....	.....	..	Died from pulmonary tuberculosis
17	Stevenson: Brit. M. J. **2**: 847, 1913	Female 22 yr.	13 yr.	.....	2,750 Gm.	Two finger breadths below costal margin	.....	.....	Epistaxis menorrhagia	..	..	1,560,000	4,568	83	Splenectomy after operation; white count, 11,200
18	Erdmann, J. F., and Moorhead, J. J.: Am. J. M. Sc. **147**: 213, 1914	Female 3½ yr.	1 yr.	Brother died with large spleen	To umbilicus	One finger breadth below costal margin	Small inguinal	.....	.....	..	..	6,200,000	7,200	85	Splenectomy; patient well 10 years after operation
19	Niemann: Jahrb. f. Kinderh. **79**: 1, 1914	Female 1 yr., 5 mo.	2 mo.	.....	Less than 5 cm. below costal margin	Palpable	.....	.....	.....	+	..	Normal			Ascites; died
20	Herrmann, Roth and Bernstein: Arch. Pediat. **31**: 340, 1914	Male 14 yr.	7 yr.	Sister	1,320 Gm.	5 cm. below costal margin	Small axillary and inguinal	.....	Gums and hemoptysis	+	+	3,800,000	2,800	64	Splenectomy; living 6 weeks after operation; splenectomy on sister showed characteristic signs
21	Bruce [23]	Male 46 yr.	43 yr.	.....	5 cm. below costal margin	.....	.....	Numbness of legs	Epistaxis	+	..	3,500,000	4,800	65	Splenectomy; white cell count, 9,400; living 10 years after
22	Evans, F. A.: Proc. New York Path. Soc., June, 1916	Male 5 yr.	2 yr.	.....	350 Gm.	600 Gm.	Thymus; retroperitoneal; mesenteric	Lower one-third of femur involved	.....	..	..	.....	.....	..	Died from grand mal, petechial hemorrhages in pericardium

* Just as this tabulation was completed, a report of several new cases by Sara Welt and co-workers appeared in the literature.

TABLE 2.—*Complete Tabulation of the Cases of Gaucher's Disease Up to the Present Time*—Continued*

No.	Author	Sex and Age	Age at Onset	Familial	Spleen	Liver	Lymph Nodes	Bones	Hemorrhages	Discoloration of Skin	Eye	Blood: Red Blood Cells	Blood: White Blood Cells	Blood: Hemoglobin, %	Comment
23	Veeder and Clopton: J. Missouri M. A. **14**: 49, 1917	Male 4½ yr.	4 yr.	.....	Below umbilicus	To umbilicus	.....	.....	Epistaxis and gums	+	+	3,700,000	4,400	55	Five years after splenectomy liver was larger
24	Reuben, M. S.: New York M. J. **107**: 118, 1918	Male 2 yr.	6 mo.	Sister	Below umbilicus	Below umbilicus	.....	.....	.....	+	..	3,500,000	4,500	55	Diagnosed by splenic puncture
25	Mandlebaum [7]	Female 41 yr.	6 yr.	.....	4,250 Gm.	Below umbilicus	.....	Pain	Purpuric spots; epistaxis	+	..	3,200,000	2,000	50	Splenectomy; after operation pigmentation decreased
26	Idem	Male 37 yr.	25 yr.	.....	3,500 Gm.	2,040 Gm.	Tracheobronchial; mesenteric; peritoneal	Some involvement	Epistaxis	+	+	3,500,000	9,000	35	Splenectomy; died 17 days after operation
27	Carr and Moorhead: J. A. M. A. **72**:19 (Jan. 4) 1919	Male 46 yr.	9 yr.	.....	5 cm. below costal margin	5 cm. below costal margin	.....	.....	Gums	+	..	2,240,000	3,200	35	Splenectomy; white cell count, 9,000
28	Guyot: Ass. franç. de chir. Proc.—verb. **29**: 424, 1920	Female 43 yr.	5 yr.	.....	Below umbilicus	.....	Palpable inguinal	.....	Hemoptysis; ecchymoses	+	..	3,500,000	6,100	..	Splenectomy; white cell count, 14,000
29	Barat: Folia haemat. **26**: 223, 1920	Male 37 yr.	18 yr.	.....	2,025 Gm.	Two finger breadths below costal margin	Slight	.....	.....	..	..	5,400,000	5,600	..	Died 9 years later from pulmonary tuberculosis, pancreatitis and diabetes
30	Kraus [18]	Male 17 yr.	.....	.....	1,400 Gm.	5 cm. below costal margin	.....	.....	Epistaxis; gums	+	..	2,400,000	3,750	42	Prior to splenectomy, platelets were 60,000; 4 months after, 280,000
31	Idem.	Female 1 yr.	6 mo.	.....	70 Gm.	240 Gm.	Mesenteric; peribronchial	Some bone involvement	.....	+	..	.....	.....	..	Died from pneumonia and pleuritis
32	Rusca [17]	Male 11 mo.	8 mo.	.....	237 Gm.	390 Gm.	Tracheobronchial; cervical; inguinal	Femur and rib marrow involved	.....	+	..	3,100,000	10,000	40	Died from asphyxia
33	Keismann: Med. Klin. **17**: 1772, 1921	Female 17 yr.	9 yr.	.....	5 cm. below costal margin	Palpable	.....	.....	Petechiae	+	..	2,400,000	3,700	42	Splenectomy
34	Pool, E. H.: Ann. Surg. **74**: 625, 1921	Female 26 yr.	25 yr.	.....	Below umbilicus	.....	.....	.....	Epistaxis; ecchymoses	..	..	3,800,000	3,400	68	Splenectomy

35	Siegmund [22]	Female 9 mo.	1 wk.	Sister ?	Two finger breadths below costal margin	Two finger breadths below costal margin	.....	.....	.....	..	..		Anemia		Died from pneumonia
36	Foot and Ladd: Am. J. Dis. Child. **21**: 426 (May) 1921	Male 8 yr.	7 yr.	.....	305 Gm.	Two finger breadths below costal margin	.....	Leg pains	.....	..	..	5,800,000	6,600	90	Splenectomy; white cell count, 18,800
37	Levy: New York M. J. **113**: 586, 1921	Female 30 yr.	26 yr.	.....	Below umbilicus	Three finger breadths below costal margin	.....	.....	Epistaxis; gums	+	..	3,200,000	6,400	..	Splenectomy; death after operation
38	Kohn [19]	Female 9 mo.	.....	.....	310 Gm.	.....	Generalized	.....	.....	..	..	.....	.....	..	
39	Lippmann: Med. Klin. **18**: 1607, 1922	Female	.....	.....	Below umbilicus	Two finger breadths below costal margin	.....	.....	Epistaxis; gums; menorrhagia	..	..	4,500,000	3,200	95	Diagnosed by splenic puncture
40	Pick, L.: Verhandl. d. Berl. med. Gesellsch. **11**: 1449, 1922	Male 43 yr.	.....	Brother	1,600 Gm.	Enormous	Bronchial; perisplenic	Skeletal involvement of 11th and 12th thoracic vertebrae with gibbus	.....	..	..	.....	.....	..	Died from duct carcinoma of liver; syphilitic history; brother of patient in case 48
41	Nauwerck and Pick [20] ..	Male 8 mo.	.....	.....	80 Gm.	Not enlarged	Mesenteric	.....	.....	..	..	.....	.....	..	Died of bronchopneumonia
42	Harvier and Lebec: Bull. et mém. Soc. méd. d. hôp. de Paris **47**: 87, 1923	Female 20 yr.	13 yr.	Sister	Below umbilicus	.....	.....	.....	Menorrhagia	..	..	.....	.....	..	Fifteen months after operation (splenectomy): red blood cells, 4,900,000; white blood cells, 4,900; hemoglobin, 80%, with normal bleeding and clotting time
43	Fahr and Stamm: Monatschr. f. Kinderh. **26**: 169, 1923	Male 3 yr.	2 yr., 10 mo.	.....	Below umbilicus	Three finger breadths below costal margin	.....	.....	Epistaxis	+	..	2,000,000	5,800	30	Died from hemorrhage
44	Reber, M.: Jahrb. f. Kinderh. **105**: 277, 1924	Male 5 mo.	.....	Sister	.....	.....	.....	.....	.....	..	..	.....	.....	..	Diagnosed at autopsy
45	Zadek, I.: Med. Klin. **20**: 78, 1924	Male 41 yr.	30 yr.	.....	1,250 Gm.	Three finger breadths below costal margin	.....	Marrow of tibia and fibula; spontaneous fractures of humerus	Gums; hematemesis; petechiae	+	+	4,200,000	5,800	75	Normal fragility and clotting time; died from pneumonia
46	Epstein [13]	Female 51 yr.	.....	.....	Very large	Very large	.....	.....	.....	..	..	3,100,000	3,200	48	Died from leptomeningitis and lobar pneumonia

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TABLE 2.—*Complete Tabulation of the Cases of Gaucher's Disease Up to the Present Time*—Continued*

No.	Author	Sex and Age	Age at Onset	Familial	Spleen	Liver	Lymph Nodes	Bones	Hemorrhages	Discoloration of Skin	Discoloration of Eye	Blood: Red Blood Cells	Blood: White Blood Cells	Blood: Hemoglobin, %	Comment
47	Epstein, E.: Virchows Arch. f. path. Anat. u. Physiol. **253**: 157, 1924	Male 30 yr.	.....	.....	1,900 Gm.	2,900 Gm.	Moderately enlarged	Vertebral involvement with typical cells	.....	..	..	.....	.....	..	Died from ulcerocaseous pulmonary tuberculosis and peritonitis
48	Pick, L.: Med. Klin. **20**: 1526, 1924	Male 56 yr.	.....	Brother	1,160 Gm.	2,180 Gm.	Supraclavicular; mesenteric; peripancreatic moderately involved	Osteoporosis involving ninth thoracic vertebra with gibbus	.....	..	..	.....	.....	..	Died from tubercular peritonitis and pleuritis; brother of patient in case 40
49	Reber, M.: Jahrb. f. Kinderh. **105**: 277, 1924	Female 5 mo.	.....	Sister	Two finger breadths below costal margin	Two finger breadths below costal margin	.....	.....	Hematemesis	..	..	4,000,000	11,800	62	Died from hemorrhagic pachymeningitis; necropsy on sister but no definite diagnosis made
50	Epstein, E.: Wien. klin. Wchnschr. **37**: 1179, 1924	Female 28 yr.	.....	Sister	1,600 Gm.	.....	.....	.....	.....	..	..	.....	.....	..	Sister of patient in case 51
51	Idem.	Female 35 yr.	.....	Sister	1,830 Gm.	.....	.....	.....	.....	..	..	.....	.....	..	Splenectomy; died of pulmonary tuberculosis; sister of patient in case 50
52	Waugh and MacIntosh: Arch. Int. Med. **33**: 599 (May) 1924	Female 5 yr.	3 yr.	.....	345 Gm.	Palpable	.....	.....	.....	+	..		Leukopenia		Splenectomy; month after operation, liver smaller
53	Moscheowitz, E.: Proc. New York Path. Soc. **24**: 18, 1924	Female 15 yr.	.....	Sister	1,940 Gm.	.....	.....	.....	.....	..	..	.....	.....	..	Following splenectomy osteomyelitis of femur occurred
54	Reuben [15]	Male 15 yr.	.....	.....	Below umbilicus	Below umbilicus	.....	.....	Epistaxis	+	..	4,100,000	3,900	64	Diagnosed by splenic puncture; normal fragility and clotting time
55	Schuster, N. H.: Lancet **2**: 170, 1924	Female 22 mo.	18 mo.	.....	Below umbilicus	.....	Small axillary and perisplenic involvement	.....	Petechiae	+	..	1,200,000	14,900	28	Polychromatophilia with many myelocytes; died from acute edema of lungs
56	Mienzil, K.: Med. Klin. **20**: 935, 1924	Female 48 yr.	.....	.....	750 Gm.	.....	Calcareous changes in tracheobronchial group	.....	.....	..	..	.....	.....	..	Died from chronic adhesive tubercular peritonitis with miliary tuberculosis

57	Pick: Med. Klin. **21**: 441, 1925	Female 40 yr.	15 yr.	.....	1,100 Gm.	.....	.....	.....	Hemoptysis; purpura; gums	..	..	5,000,000	7,000	106	15,000 platelets; these increased following splenectomy; died from pulmonary infarcts
58	Bloom, W.: Am. J. Path. **6**: 505, 1925	Male 6 yr.	.....	.....	650 Gm.	.....	.....	.....	Epistaxis for 3 years	..	..	.....	.....	..	Splenectomy with increase of red and white blood cells and hemoglobin
59	Idem.	Female 42 yr.	.....	.....	742 Gm.	.....	.....	.....	.....	..	..	.....	.....	..	
60	Howland and Rich: Johns Hopkins Hospital, 1925	Female 13 yr.	.....	.....	Expirated at 18 months	Enlarged after splenectomy	General involvement	Osteoporosis; two spontaneous fractures of femur; compression of vertebrae	.....	..	..	.....	.....	..	Growth of Gaucher cells around nerve roots and in spinal canal
61	Smith, L.: Children's Hospital, Boston, 1925	Female 2 yr., 7 mo.	1 yr., 7 mo.	.....	Below umbilicus	Three finger breadths below costal margin	.....	.....	.....	+	..	3,520,000	4,200	55	Splenectomy; died from peritonitis 11 days after operation
62	Horax, G.: Peter Bent Brigham Hospital, Boston, 1925	Female 13 yr.	6 yr.	.....	To iliac crest	Three finger breadths below costal margin	Glands in left axilla	.....	.....	..	..	3,328,000	4,400	65	Splenectomy; white blood cells, 13,100; biopsy of cervical gland showed typical cells
63	Cushing and Stout [9]...	Female 29 yr.	.....	.....	999 Gm.	Two finger breadths below costal margin	.....	.....	Epistaxis	+	+	5,440,000	5,600	90	Increasing pigmentation following splenectomy
64	Idem.	Female 33 yr.	32 yr.	Brother (?)	1,017 Gm.	Just palpable	.....	Shortening of right leg; pain in hip	Epistaxis; gums; menorrhagia	+	+	1,330,000	2,900	23	Splenectomy; white blood cells, 8,900; resection of head and neck of right femur showed Gaucher cells
65	Harper, W. W.: South. M. J. **19**: 746, 1926	Female 18 yr.	.....	Brother (?)	Three finger breadths below costal margin	Palpable	.....	.....	.....	+	..	3,700,000	8,100	65	Splenectomy; brother is a spastic paraplegia with enlarged spleen
66	Hara, H., and Guido, F.: California & West. Med. **25**: 215, 1926	Female 4 yr.	3 yr.	Brother (?)	Below umbilicus	Three finger breadths below costal margin	.....	.....	Epistaxis; gums; purpura	+	..	2,980,000	7,000	30	Splenectomy; 40 days after, white blood cells, 15,200
67	Warren [28]	Female 26 yr.	8 yr.	.....	2,100 Gm.	.....	.....	.....	.....	+	..	5,000,000	5,000	64	Epigastric pain; splenectomy; 3 years after gave birth to child; no enlargement of liver

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TABLE 2.—*Complete Tabulation of the Cases of Gaucher's Disease Up to the Present Time*—Continued*

No.	Author	Sex and Age	Age at Onset	Familial	Spleen	Liver	Lymph Nodes	Bones	Hemorrhages	Discoloration of Skin	Eye	Blood: Red Blood Cells	Blood: White Blood Cells	Blood: Hemoglobin, %	Comment
68	Santee, H.: Ann. Surg. **86**: 707, 1927	Male 29 yr.	1 yr.	Brother	2,600 Gm., to anterior border of pelvis	To umbilicus	.....	Left hip resembled tuberculous involvement; head of femur mottled	.....	..	+	2,700,000	2,700	48	Condition began with pain in right hip; splenectomy; 6 months later, white blood cells 8,700; brother of patient in case 69
69	Idem.	Male 31 yr.	22 yr.	Brother	To umbilicus	To umbilicus	.....	.....	Epistaxis	..	+	.....	5,200	60	Complains of abdominal pain; brother of patient in case 68
70	Moro and Clairmont (not published)	Male 13 yr.	11 yr.	.....	Below umbilicus	.....	.....	.....	.....	..	..	4,000,000	2,800	65	Splenectomy
71	Moro and Clairmont (not published)	Male 9¾ yr.	5 yr.	.....	Large spleen	.....	.....	.....	Epistaxis	..	..	4,400,000	2,300	45	Splenectomy; white blood cells, 32,000; hemoglobin normal
72	Klucker and Petren: Acta paediat., 1927, vol. 6	Female 3 yr.	1 yr.	.....	1,150 Gm.	.....	.....	.....	Petechiae	..	..	.....	3,101	50	Splenectomy; bone trouble 1½ years later; white blood cells, 12,436; hemoglobin, 70%
73	Fischer, A. W.: Beitr. z. klin. Chir. **141**: 200, 1927	Female 45 yr.	26 yr.	.....	1,000 Gm.	.....	.....	.....	Epistaxis; gums	..	..	3,500,000	7,400	80	Splenectomy; 4 weeks later red blood cells, 4,200,000; white blood cells, 15,000
74	Weltman and Deuticke: Wien. klin. Wchnschr. **40**: 937, 1927	Female 17 yr.	.....	.....	.....	.....	Generalized parotids enlarged	.....	.....	+	+	.....	3,500	..	Thrombopenia
75	Lindau, A.: Acta path. et microbiol. Scandinav. **5**: 22, 1928	Female 3 yr.	.....	.....	1,100 Gm.	Enlarged	.....	Left hip involved	Purpura	..	..	.....	2,600	..	Splenectomy followed by hip joint flare up; roentgenogram similar to tuberculous joint
76	Oberling and Woringer,[16] case 1.....	Male 10 mo.	7 mo.	Brothers and sister	.....	.....	Cervical submaxillary	.....	.....	..	..	.....	.....	..	Distended abdomen; brother of patients in following three cases; neurologic symptoms predominated
77	Idem., case 2.....	Male 11 mo.	.....	Brothers and sister	To symphysis	To umbilicus	.....	.....	.....	..	..	5,190,000	11,300	..	Diagnosis made at autopsy
78	Idem., case 3.....	Female 5 mo.	.....	Brothers and sister	Two finger breadths below costal margin	Palpable	General	.....	.....	..	..	4,400,000	6,300	54	Platelets, 66,000; marked neurologic symptoms; died at 8 months; autopsy confirmed diagnosis

79	Idem., case 4	Male 1 mo.	.....	Brothers and sister	Palpable	Palpable	.....	.....	.....			4,350,000	5,700	75	Neurologic symptoms; autopsy confirmed diagnosis
80	Graham and Blacklock,[29] case 1	Female 1½ yr.	11 mo.	.....	To iliac crest, 500 Gm.	Three finger breadths below costal margin	.....	.....	Gums	+	..	2,090,000	8,600	20	Diagnosis made at autopsy
81	Idem., case 2	Male 6 yr.	4½ yr.	Brother	Two finger breadths below costal margin, 239 Gm.	Four finger breadths below costal margin	.....	.....	Gums	..	..	.....	.....	..	Diagnosis by splenic puncture; brother of patient in case 82
82	Idem., case 3	Male 10 yr.	9½ yr.	Brother	To iliac crest, 744 Gm.	Four finger breadths below costal margin	.....	.....	Gums	..	..	6,740,000	6,600	82	Splenectomy; brother of patient in case 81; pain in lower left quadrant; cyanosis and clubbing of fingers
83	Idem., case 4	Female 10 yr.	8½ yr.	. .....	Four finger breadths below costal margin, 383 Gm.	Palpable	.....	.....	Gums	..	..	3,520,000	6,400	62	Began with fever and jaundice
84	Idem., case 5	Female 35 yr.	.....	(?)	2,490 Gm.	Palpable	.....	.....	.....	+	..	.....	.....	..	Sister had an enlarged spleen
85	Muhsam, R.: Deutsche med. Wchnschr. **54**: 551, 1928	Male 27 yr.	7 yr.	.....	900 Gm.	Two finger breadths below costal margin	.....	.....	Petechiae	+	..	2,930,000	1,400	65	Splenic tenderness with intermittent attacks of jaundice; splenectomy, but still had jaundice
86	Idem.	Female 32 yr.	.....	.....	To umbilicus	One finger breadth below costal margin	.....	.....	Epistaxis; purpura; menorrhagia	+	.	4,250,000	3,200	86	Platelets, 180,000; splenectomy
87	Davidsohn, L. W.: Arch f. klin. Chir. **150**: 537, 1928	Male 9 yr.	5 yr.	.....	Three finger breadths to right of midline, 1,915 Gm.	Four finger breadths below costal margin	.....	.....	Epistaxis	..	..	2,900,000	3,200	53	Splenectomy; 2 months after operation white blood cells, 7,800; 1 year after operation, white blood cells, 9,400
88	Hess, Julius H.: Sarah Morris Hospital, 1929 (not published)	Male 2 yr., 8 mo.	3 mo.	.....	To umbilicus, 650 Gm.	Two finger breadths below costal margin	Palpable cervical	.....	Purpura	+	+	4,100,000	4,300	70	Biopsy of liver showed Gaucher's cells; splenectomy; 6 months after liver was four finger breadths below costal margin; white blood cells, 24,000; cervical and submental glands prominent
89	Authors' case	Male 1 yr., 5 mo.	?	.....	To umbilicus	Below umbilicus	General	.....	.....	..	..	4,000,000	26,000	70	Diagnosis made by section of inguinal gland

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per cent monocytes, 0.5 eosinophils. Three normoblasts, one microblast, one myelocyte, two megaloblasts and two metamyelocytes were seen. The red cells showed marked poikilocytosis and anisocytosis. There was marked acromia with moderate reticulocytosis.

Roentgenologic examination of the upper and lower extremities and upper part of the spine was made and the following noted (fig. 2): (1) marked periosteal proliferation and calcium deposition along the humeri, femora, tibiae and fibulae; (2) tendency to coarse vacuolization of the bony structure; (3) bowing of the femora, tibiae and fibulae; (4) transverse striations at the metaphyseal ends of the long bones, and (5) areas of rarefaction immediately adjacent to the metaphyseal ends of the long bones.

The observations are those typically observed in cases of rachitis (healed). There was no evidence of the signs seen in many cases of Gaucher's disease, such as fusiform enlargement of lower femora and mottling of the bone-marrow.

Biopsy of an inguinal gland was made on February 1, and the pathologic report by Dr. Richard H. Jaffe, chief pathologist, Cook County Hospital, was as follows:

The lymph gland was ovoid and soft, with a thin capsule. It consisted of a light yellow-gray tissue with a narrow peripheral rim which was darker gray and slightly transparent.

In microscopic sections most of the lymphatic tissue appeared replaced by large, pale-stained, round or oval cells. In the periphery a small zone of lymphoid tissue was left, which showed a poorly defined differentiation into follicles. The large cells seemed to proliferate from the medullary portion encroaching on the narrow marginal zone of lymphatic tissue. The cells were arranged in alveoli, the intervening tissue being formed by the compressed sinuses, the endothelium of which was flat and did not take part in the formation of the large cells. In the lumen of the sinuses there were a few lymphocytes.

The finer morphology of the large cells was as follows: The cytoplasm was crossed by a delicate network of parallel and wavy lines (fig. 1). These lines stained distinctly blue with Mallory's aniline blue solution, while the substance between the fibers assumed a pale blue hue. There were one or two nuclei which were small and round or oval. They had a distinct membrane and a scanty finely granular chromatin structure. There was a small slightly oxyphilic nucleolus. The nuclei were usually located near the periphery of the cells.

In the cortical zone of lymphatic tissue, the origin of the large cells could be traced to the reticulum cells. They became round and swollen, and the cytoplasm became differentiated into fine lines. There remained between the cells a fine network of fibrils which radiated from the adventitia of the small blood vessels. The marginal sinus was narrow, and its endothelium was flat.

Staining with sudan III and with Lorrain Smith's lipoid stain revealed no lipoid material in the cells. There was a small amount of hemosiderin which, however, showed no relation to the large cells.

The anatomic diagnosis was Gaucher's disease.

Splenic puncture was done on the same date, and a wet smear showed typical Gaucher cells, which were most distinct in the unstained preparation. Stained specimens did not reveal these cells intact, indicating that they are extremely fragile.

Course.—During the patient's sojourn in the hospital, he had a septic temperature varying from 102 to 105 F.; a pulse rate of 100 to 140 and a respiratory rate of from 20 to 50. The left ear drained profusely. The cervical glands remained about the same size. The child became progressively worse, lost weight, developed bronchopneumonia and died fifteen days after admission. Permission for autopsy could not be obtained.

COMMENT

There are a few features in this case that differ somewhat from the typical case. The markedly enlarged glands on the left side of the neck presented an unusual picture for this condition. Whether this marked cervical adenopathy was due to the left otitis media, to the disease or to both is not definitely known. Although the enlarged inguinal gland was unusual of such a gland, biopsy definitely showed the typical picture. Welt [30] has recently stated that peripheral glands are rarely involved. The marked leukocytosis can readily be explained by the coexisting otitis media. As the child was colored, no pigmentation was discernible. It is interesting to compare the blood lipoid content with that in Niemann-Pick's disease (table 1).

DIAGNOSIS

The diagnosis frequently can be established by one of the following procedures: (1) biopsy of a peripheral gland; (2) splenic puncture; (3) bone-marrow puncture, or (4) roentgenologic examination of the bones.

In a differential diagnosis, one must consider all causes for splenomegaly, chiefly Niemann-Pick's disease, Banti's disease, Hanot's cirrhosis, von Jaksch's anemia, malaria, amaurotic familial idiocy, hemolytic jaundice, leukemia and Hodgkins' disease, and in the osseous type, tuberculosis and syphilis.

SUMMARY

Eighty-nine cases of Gaucher's disease are tabulated and reviewed. A case diagnosed by biopsy of a peripheral lymph gland is reported.

SUPPURATIVE EPIDIDYMITIS IN INFANCY*

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Although of infrequent occurrence in infancy, epididymitis is a lesion which must be considered in the differential diagnosis of scrotal swellings in the young. The following case is reported not only to direct attention to the clinical picture and diagnosis of this condition, but to note the similarity of the symptoms, physical observations and treatment for the disease as it occurs both in infants and in adults.

REPORT OF CASE

E. C., aged 22 months, was admitted to the hospital on Feb. 22, 1929, with the complaint of pain and swelling of the right side of the scrotum. Four weeks previously, after not having urinated for a period of from seven to eight hours, voiding was followed by terminal hematuria. Slight frequency and burning on urination developed. One week later, the right side of the scrotum became tender and swollen and continued to enlarge until the time of admission to the hospital. Dysuria increased, so much so that the child cried out with each urination. With the progressing severity of the local symptoms, the family physician became alarmed and referred the child to the hospital. At no time was a urethral discharge present. There was nothing in the past or family history relevant to the present condition.

Physical examination revealed enlarged cervical glands as well as markedly hypertrophied infected tonsils. The remainder of the physical examination was negative, except for an enlargement of the right side of the scrotum to six times the normal size, the overlying skin being dusky red with a small yellowish area of early cutaneous gangrene over the anterior scrotal surface. The inflammatory mass was acutely tender, and the subcutaneous fluctuation of an abscess was elicited anteriorly. Because of the solidity of the scrotal mass, the testis and epididymis could not be anatomically differentiated. The spermatic cord was enlarged to twice the normal size, and was tender and indurated. Rectal examination revealed marked induration and swelling of the right side of the prostate and region of the right seminal vesicle. The results of urinalysis were negative, as was the Wassermann reaction. The blood showed: red cells, 4,070,000; leukocytes, 13,600, with 68 per cent polymorphonuclear cells. A preoperative diagnosis of suppurative epididymitis with secondary involvement of the testis was made, and operation was advised.

With the patient under open drop ether anesthesia, incision over the right scrotal mass revealed an abscess of moderate size. The testicle was delivered. This mass was three times the normal size and was firmly indurated. The tunica albuginea and tunica vaginalis were densely adherent to each other throughout. In the inflammatory mass the epididymis and testicle were firmly bound together

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* From the Pediatric Service of the New York Nursery and Child's Hospital.

and could not be differentiated. Incision in three areas over the testicular mass revealed free pus. Believing that I was dealing with a secondary suppurative orchitis, orchidectomy was performed. Scrotal drains were removed after twenty-four hours; the temperature was normal after one week, and the child was discharged on the ninth day with the operative wound well healed.

The pathologic report was made by Dr. James R. Wilson. A culture taken from the epididymis at the time of operation showed a pure culture of *Staphylococcus aureus.*

The gross specimen consisted of an enucleated testicle and an epididymis measuring 3.2 cm. in its greatest diameter. On section, the gray testicular tissue was found at one end. This was grossly normal and was surrounded by a smooth, gray, glistening tunica. Above the testicle the epididymis was markedly swollen, and in its substance there were a number of small abscesses from which thick yellow pus could be expressed.

Microscopic examination showed that the testicle and surrounding tunica were normal. In the connective tissue supporting the epididymis there were several

Surgical specimen from the case reported. The normal, somewhat compressed testis is noted. The remainder of the mass is the indurated suppurating epididymis. Because of marked shortening of the spermatic cord by inflammatory infiltration, amputation of the mass was performed rather close to the testicle.

small abscesses filled with pus cells and nuclear debris. The adjacent tissue was irregularly infiltrated with leukocytes. Among these were numerous eosinophils and a moderate number of polymorphonuclears. The testicular structures were almost entirely free from exudate.

The diagnosis was acute epididymitis.

COMMENT

Obviously, the epididymitis in this case was secondary to an acute prostatitis. The organisms (staphylococci) may have reached the prostate directly through the blood stream or may have lodged there following their elimination into the urine from the kidney. The most likely primary bacterial focus was the severely infected tonsils. Such

bacterial metastases to the prostate from the upper respiratory tract have been observed frequently in adults.

In the acute stage, epididymitis is a catarrhal or exudative process accompanied by cloudy swelling and desquamation of the cylindric epithelial lining of the tubules, with intense leukocytic infiltration of the lumina and interstitial tissues. As the process advances, tubular destruction ensues and minute focal abscesses are formed; these, unless resolution occurs at this stage, coalesce and result in the formation of a gross abscess. Extension of the latter condition may involve the spermatic cord by bringing about inflammatory thrombosis or may secondarily invade the testis with ultimate destruction of the organ.

When the lesion does not progress to gross suppuration, healing occurs by resolution and sclerosis. As a result of the scarring, many tubules become blocked off and many disappear, and the likelihood of sterility in the involved side is great.[1]

Pain and swelling are the outstanding symptoms of epididymitis. When the process is acute, the patient will scarcely permit palpation of the affected organ. Not infrequently pain reference along the spermatic cord to the groin causes marked lower abdominal discomfort. Swelling usually accompanies the disease; the scrotum often enlarges from five to six times the normal size. Changes in the skin—redness and edema—are secondary to the underlying infection. In the presence of acute hydrocele, the scrotal mass may be extremely large and hard. Because of the tenseness of the hydrocele mass, fluctuation is rarely made out. Fever is usually present but is rarely high, except in the presence of marked general toxemia. Other manifestations of this toxemia are nausea, vomiting, anorexia and drowsiness.

At the onset of the epididymitis, anatomic differentiation between the swollen tender epididymis and the normal softer testis is easily made, except in the presence of hydrocele. This differentiation is most important, as it enables one to distinguish correctly between epididymitis and true orchitis (of mumps, typhoid, etc.). This differentiation is essential, not only for the establishment of the correct diagnosis, but for the proper treatment for these respective diseases. While true orchitis rarely terminates in suppuration and is a more or less self-limited disease, approximately one in every four cases of nongonorrheal, nontuberculous epididymitis suppurate and, if neglected, may lead to loss of the testicle by secondary necrotic involvement.[2] One in every fifteen cases of gonococcus epididymitis terminate in gross abscess.[3]

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1. Campbell, M. F.: The Surgical Pathology of Epididymitis, Ann. Surg. **88**:98 (July) 1928.

2. Campbell, M. F.: Non-Gonorrheal Non-Tuberculous Epididymitis, Am. J. M. Sc. **176**:386 (Sept.) 1928.

3. Campbell, M. F.: Gonococcus Epididymitis, Ann. Surg. **86**:577 (Oct.) 1927.

In the presence of an associated urethral discharge, the organisms found in the exudate establish the bacterial etiology of the epididymitis. The most frequently found organisms are gonococci, staphylococci, streptococci, *Micrococcus catarrhalis* and *B. coli*. A few cases of gonococcus epididymitis in somewhat older boys have been reported, as have instances of tuberculous epididymitis. In all types of epididymitis, involvement of the spermatic cord and prostate, as well as either or both seminal vesicles, is commonly found. By rectal palpation with the little finger, one may easily and painlessly determine the size, contour and consistency of the prostate and vesicles.

The value of rectal examination in all cases of scrotal swellings cannot be overstressed. Absence of prostatic and vesicle involvement rather indicates that epididymitis is not present. With torsion of the spermatic cord, the lesion which most clearly simulates epididymitis, the upper scrotal spermatic cord, prostate and vesicles are normal. This is an important point, since several cases of torsion have been observed in infancy and in childhood.[4]

When the diagnosis of acute epididymitis has been established, the treatment is elevation and support of the scrotal contents. This is best accomplished by the use of the adhesive scrotal suspensory, which I have described elsewhere.[5] An ice cap locally makes the patient more comfortable. If, after from forty-eight to seventy-two hours of this treatment pain is severe enough to prevent sleep, or there is evidence of marked secondary toxemia, epididymotomy is indicated. The essential feature of this procedure is multiple puncture with drainage of the involved epididymis.[5] This operation will at once relieve the pain and general symptoms and, in not a few cases, will prevent secondary suppurative involvement and loss of the testicle. As in the case reported, long-standing suppuration of the epididymis leads to involvement of the overlying skin, often terminating in cutaneous gangrene with extrusion of the testicle. It is probable that in another week testicular extrusion would have occurred in this patient, as cutaneous gangrene had already set in. Early and correct diagnosis is therefore imperative, not only to insure proper treatment for the epididymal involvement but to prevent secondary extension to the testicle with grave danger of loss of this organ. Epididymotomy is attended by little surgical risk and may be the means of saving the testis. In my case, because of the somewhat long duration and the extent of the suppurative process, anatomic differentiation between testis and epididymis was impossible; the explora-

4. Campbell, M. F.: Torsion of the Spermatic Cord, Surg. Gynec. Obst. **44**:311 (March) 1927.

5. Campbell, M. F.: Treatment of Acute Epididymitis, J. A. M. A. **89**:2108 (Dec. 17) 1927.

tory incisions into the inflammatory mass always revealed free pus, erroneously leading to the conclusion that suppurative orchitis also existed. The testicle was therefore removed.

If the epididymitis subsides with the application of the scrotal suspensory (as most often occurs), the dressing may be removed at the end of one week. It should be noted that internal medications are of no curative value in the treatment for this lesion; opiates will relieve pain.

SUMMARY

The case of a patient with suppurative epididymitis who was treated surgically is reported. Although epididymitis is commonly observed in adults, the disease is of rare occurrence in infancy. The etiologic, pathologic, symptomatic, diagnostic and therapeutic phases of the disease as it occurs in infants and adults are similar in all respects. Differentiation between involvement of the epididymis and of the testicle is usually easily accomplished by palpation. The importance and value of rectal examination in these cases cannot be overemphasized. Elevation and support of the scrotal contents are the indicated palliative treatment. Failure of this measure to bring about relief from pain or subsidence of systemic symptoms within seventy-two hours indicates epididymotomy. A liberal surgical attitude is advised, since the operation entails relatively small risk and may save the testicle from secondary suppurative involvement with subsequent loss of the organ.

HORSESHOE KIDNEY *

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Horseshoe kidney is an unusual anomaly. Morris [1] reported one incidence in 1,590 autopsies; Küster,[2] one in 1,100; Botez,[3] one in 715, and Eisendrath,[4] one in 800. In 68,000 postmortem examinations, Carlier and Gérard [5] reported one incidence in 850; Judd, Braasch and Scholl [6] recorded 17 horseshoe kidneys in 2,424 operations on the kidney. These authors stated that the usual position for this anomaly is median and caudad to the normal. The masses of kidney tissue tend to converge downward and inward, responding to the traction exerted by the commissure on the anterior poles. In the secondary development, fusion of the kidneys prevents complete rotation on the vertical axis, leaving the pelves facing anteriorly. In most cases, the pelves are extrarenal and deficient in support of the enveloping tissue.

In the majority of cases of horseshoe kidney, the fusion occurs at the lower poles. In 262 cases, Beyer [7] reported 18 with fusion of the upper pole. This fusion is usually anterior to the great vessels, and the isthmus usually contains glomeruli and tubules. Taylor [8] reported 7 per cent and Gérard [9] 8 per cent of cases with fusion of the upper poles; Marion,[10] however, stated that only twelve cases have actually been

* Submitted for publication, May 15, 1929.
* From the Milwaukee Children's Hospital.

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2. Küster: Chirurgie der Niere, in Deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1896-1902.

3. Botez, G.: Considération sur la pathologie et la chirurgie du rein en fer à cheval, J. d'urol. **1**:193, 373, 503 and 633, 1912.

4. Eisendrath, D. N.; Phifer, F. M., and Culver, H. B.: Horseshoe Kidney, Ann. Surg. **82**:735, 1925.

5. Carlier, V., and Gérard, M.: Anatomie chirurgicale et chirurgie du rein en fer à cheval, Rev. de chir. **46**:9 and 196, 1912.

6. Judd, F. S.; Braasch, W. F., and Scholl, A. J.: Horseshoe Kidney, J. A. M. A. **79**:1189 (Oct. 7) 1922.

7. Beyer, C.: Le rein en fer à cheval, Arch. internat. de chir. **5**:517, 1912.

8. Taylor, K. P. A.: Am. J. M. Sc. **161**:238, 1921.

9. Gérard, M.: Anatomie chirurgicale et chirurgie du rein en fer à cheval, Rev. de chir. **46**:9 and 196, 1912.

10. Marion, G.: Traité d'urologie, Paris, Masson & Cie, 1928.

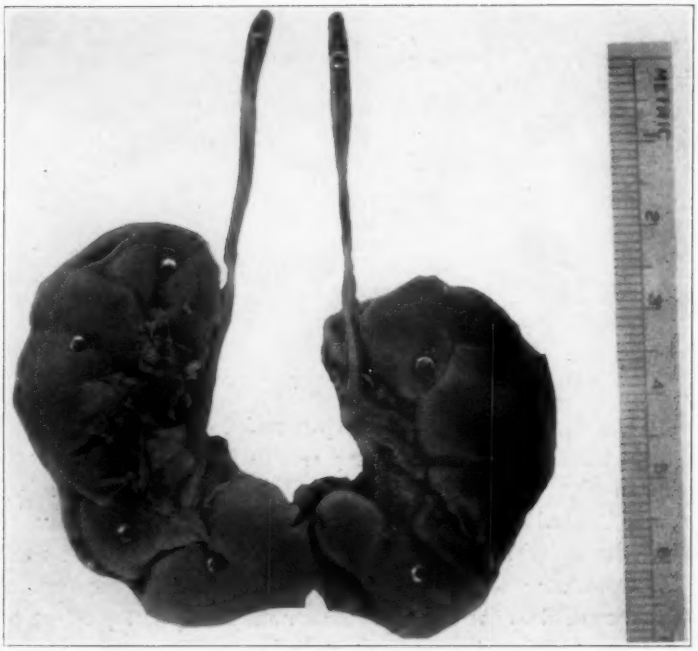

Fig. 1.—Specimen of kidney fastened with pins.

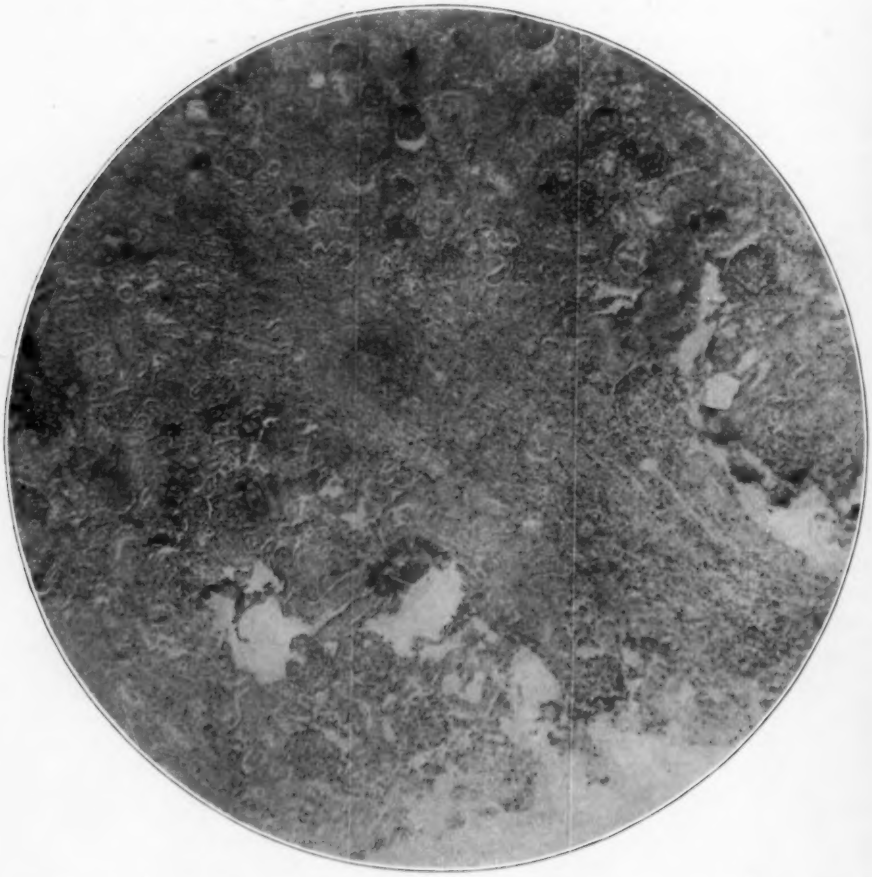

Fig. 2.—Section through the isthmus, showing the glomeruli and tubules; low power.

described. The only cases with which we are familiar are those of Karewski,[11] Robinson [12] and Newman.[13]

The infrequency of fusion of the upper poles is easily explained by a study of the embryologic development. About the fourth week of fetal life, when the metanephros begins to ascend from the pelvis toward the lumbar fossa, there is an internal rotation and a deviation of the

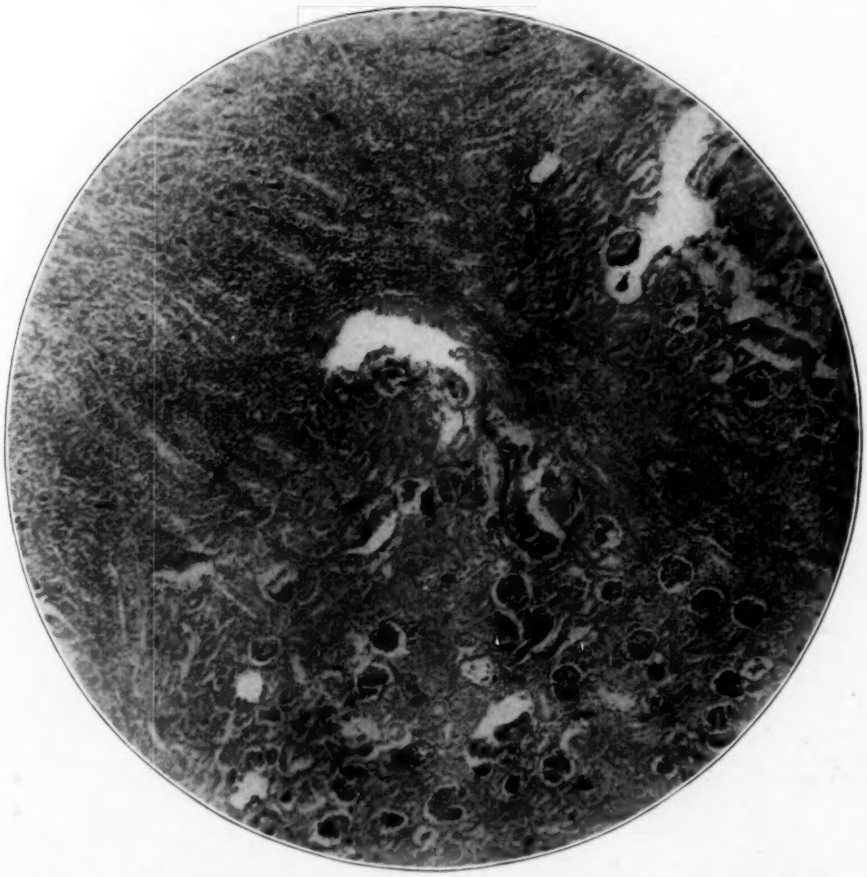

Fig. 3.—Section through the isthmus, showing the glomeruli and tubules; low power.

upper poles. In the pelvis the longitudinal axis of the kidney is practically perpendicular, and the pelvis faces anteriorly. In the ascent the longitudinal axis becomes oblique and the lower poles approach each

11. Karewski: Deutsche med. Wchnschr. **47**:989, 1921.

12. Robinson, B.: The Ureter in Fused (Horseshoe) Kidney, Am. J. Urol. **4**:121, 1908.

13. Newman, D.: Lancet **2**:236, 1917.

other, so much so that they come in contact and, in most cases of horseshoe kidney, fuse at this time. Thus, fusion of the kidneys at the upper pole must take place before the fourth week of fetal life. Theoretically, therefore, the isthmus should always consist of parenchyma of the same character as that found throughout the rest of the fused organ. This is found in 85 per cent of cases, and in the other 15 per cent the isthmus

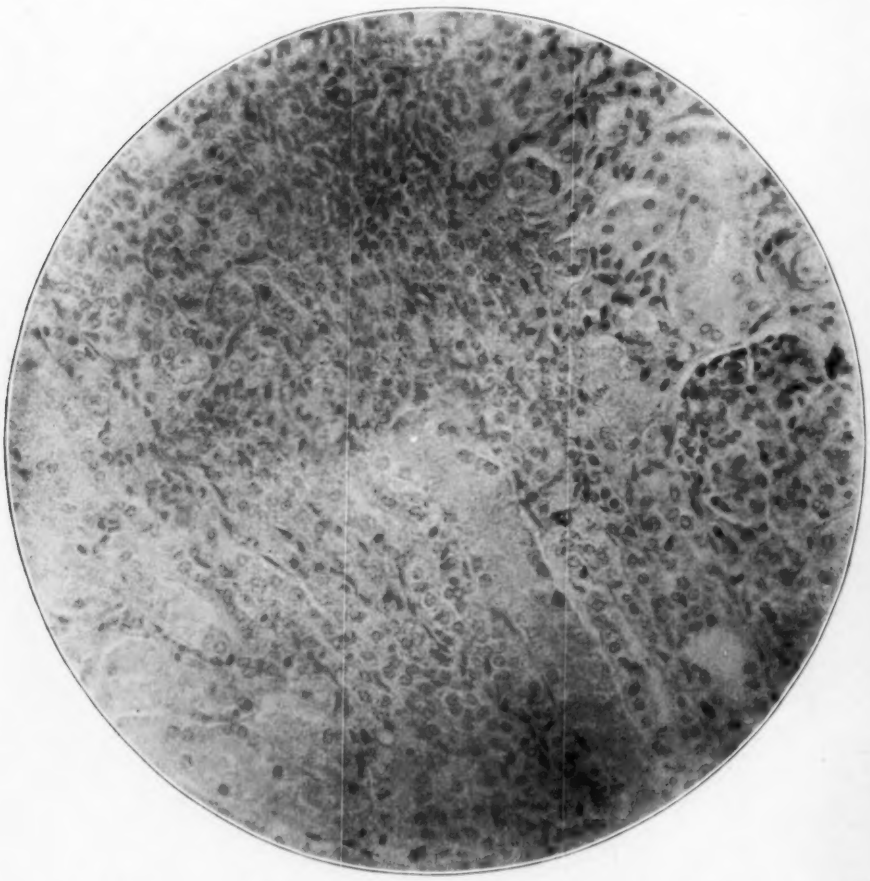

Fig. 4.—Section through the isthmus, showing the cloudy swelling of the tubules; high power.

consists of fibrous tissue. The pelves in this type face anteriorly because the early fusion prevents rotation posteriorly.

A boy, aged 37 days, was admitted to the hospital with a condition diagnosed as pyloric stenosis. There was no history of symptoms referable to the urinary tract. Physical examination revealed a tumor mass and peristaltic waves in the epigastrium. The urine showed an albumin content of 3 plus and a trace of sugar, but no other abnormalities. The patient had been vomiting for two weeks

and had had diarrhea. His birth weight was 7 pounds and 3 ounces (3.29 Kg.), and his weight at the time of admission was 6 pounds and 6 ounces (2.88 Kg.). A Fredet-Ramstedt operation was done on the third day after admission, but the patient died six days later.

Autopsy revealed the pyloric tumor with an incision through the hypertrophied muscle and the mucosa. There was a small accessory spleen 0.5 cm. in diameter. The suprarenals weighed less than 5 Gm. each, and appeared normal. They were found on the lower poles of the kidneys. The kidneys were situated in the normal position, but there was a fusion of the upper poles. The kidney mass weighed 25 Gm., and measured 4.3 cm. in width across the isthmus (fig. 1). Each kidney measured 3 cm. at its widest portion, and was 1.5 cm. in thickness. The isthmus was 1.5 cm. in diameter, and lay anterior to the great vessels. The hilum of each kidney presented a marked increase in length, and lay in the anteroposterior position. The renal pelves also faced anteriorly instead of medially, and occupied a superior position in the hilum. The left pelvis received three large calices, the inferior being the largest. The right pelvis received two calices, the larger being also inferior. The vascular pedicle occupied the inferior part of the hilum.

Section through the isthmus showed glomeruli and tubules (figs. 2 and 3). There was cloudy swelling of the tubules (fig. 4).

This case represents the only horseshoe kidney found in 336 autopsies performed by one of us (M. G. P.) on children under 15 years of age.

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CONGENITAL VALVES OF THE POSTERIOR URETHRA *

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The importance of the obstructive uropathies is being stressed more and more as time goes on. The danger resulting when these obstructions are not recognized and removed is fully realized today, complete and accurate urologic study in urinary cases having enlightened physicians as to the gravity of this type of lesion. Formerly, the study of obstructive uropathies dealt only with cases in the adult, the possibility and frequency of this lesion occurring during infancy and childhood being completely neglected. And even in adults obstructions of this nature were overlooked, except in those in whom the condition was well advanced and who showed the gravest injury to the higher urinary tract, the result being that when the obstruction was recognized, surgical relief was out of the question.

The type of obstruction is somewhat different in the child from what it is in the adult. In the adult male benign hypertrophy of the prostate, that is, of the lateral lobes, and bars and contractures as well as carcinoma are the most frequent causes of obstruction at the neck of the bladder. The next most frequent lesions are obstructions in front of the neck, which consist of old and neglected strictures of the urethra. In the child, strictures of the anterior urethra are rare and prostatic lesions are unusually rare; so that the two most frequently encountered lesions that produce obstruction are contractures of the internal urethral orifice and congenital valves in the posterior urethra, the former being more frequently found than the latter.

By reason of the widespread interest in urologic conditions in children, the rarity of the valvular type of lesion in infancy and in childhood has been noted, and in this paper a report of three unusually interesting cases is given.

REPORT OF CASES

CASE 1.—*History.*—C. E., a boy, aged 5 years, admitted to the Presbyterian Hospital, Nov. 12, 1928, and referred by Dr. William Hibbs, presented the complaints of difficulty in passing urine, the passage of a small stream, and urgency and frequency of urination, all of which dated from birth. Frequency was more

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* From the Presbyterian Hospital and the Children's Memorial Hospital.

pronounced during the forenoon, the intervals ranging from ten to twenty minutes. During the remainder of the day the child urinated from three to four times.

Examination.—Nothing of importance was found except a suprapubic tumor about the size of a large grapefruit. The daily urinalysis showed from 30 to 50 pus cells per cubic millimeter. Examination of the blood on Nov. 12, 1928, showed: red blood cells, 4,690,000; leukocytes, 6,200, and hemoglobin, 90 per cent. The blood pressure was: systolic, 110; diastolic, 80.

A blood chemical determination on Nov. 13, 1928, showed: urea nitrogen, 17.8; uric acid, 2.7; creatinine, 1.1, and nonprotein nitrogen, 41.7. The Wassermann reaction of the blood was negative.

A small cystoscope entered the bladder without difficulty or obstruction. Examination gave completely negative results. There was no evidence of disease around the internal urethral orifice. It was impossible to pass a no. 16 curved sound through the prostatic urethra.

Roentgen examination of the spine showed the absence of spina bifida occulta. The cystogram was negative, showing a normal bladder that was relatively large for the size and age of the patient. The urethrogram showed dilatation beyond the junction of the prostatic and membranous urethra. In front of this apparent obstruction the urethra measured 5 mm. and behind it, 8 mm.

A preoperative diagnosis of congenital valves of the posterior urethra was made.

Operation.—On Nov. 21, 1929, operation was performed under ethylene and ether anesthesia. In view of the fact that there was no obstruction to the entrance of the cystoscope or catheter through the urethra, it was deemed advisable to attack the obstruction through the bladder by means of a suprapubic cystotomy. The bladder wall was markedly hypertrophied. The trigone was markedly hypertrophied, and the bladder neck was seen to be wide open. A definite obstruction was palpable at the junction of the prostatic and membranous urethra. The verumontanum was felt and found to be of normal size. A no. 16 curved sound, passed from the outside, entered the bladder, but the same sound could not be passed out through the urethra from the bladder. The valves were destroyed by means of forceps, after which a no. 20 bougie was passed through the prostatic urethra. This was supplemented by sounds. By grasping the hypertrophied trigone with a Boyce tissue forceps and applying retraction, the prostatic urethra was brought into view and a normal verumontanum seen. A no. 18 plain catheter was left in the urethra and sutured to the trigone.

Result.—The patient made an uneventful recovery and left the hospital on Dec. 23, 1928. A recent report from the mother states that he is entirely free from symptoms and has no difficulty in urination.

CASE 2.—*History.*—R. J., a boy, aged 22 months, admitted to the Presbyterian Hospital, Nov. 23, 1927, was referred by Dr. A. H. Parmelee who stated that the child had an apparently normal infancy and seemed in good health until about two and one-half months before admission to the hospital, at which time he had some pain on urination and what seemed to be a chill followed by fever. Physical examination by the family physician at that time revealed nothing of importance, but the urine showed considerable pus. He made a diagnosis of pyelitis and began giving the child alkalis. However, the elevation in temperature did not subside, and after a few days evidences of a respiratory infection were found. The elevation in temperature continued, and finally, after consultation, it was decided that he had bronchopneumonia. The former urinary symptoms were lost sight of, and no further specimens were examined. During the next three or four weeks, several acute chills were recorded followed by extremely high tem-

perature. At this time a roentgenogram of the chest showed the lungs to be practically clear. Because the temperature persisted, in spite of the respiratory infection having cleared up, Dr. Parmelee was called in consultation and the result of his examination was as follows:

Examination.—The child was emaciated and extremely pale; it was restless and in evident distress. The cheeks were flushed and the body hot. Examination of the head, neck, throat, ears and chest gave negative results. When the abdomen, which was definitely distended, was palpated, a large mass was felt in the left side extending up under the costal margin and down to the brim of the pelvis. This mass was not nodular but seemed firm and tender to pressure. A somewhat similar mass, though not as large, was felt in the right side; it was also tender to pressure. There was no edema of the extremities, and all reflexes were normal.

In view of the history of pus in the urine on an earlier examination and the presence of a mass in the abdomen on either side, a probable diagnosis of hydronephrosis and pyonephrosis was made and investigation in a hospital was urged.

On more careful questioning of the parents, it was ascertained that the child was always able to pass urine more freely while lying down than in a sitting position.

Many examinations of the urine were made, the pus cells varying from 600 to 4,600 per cubic millimeter. Cultures showed *B. pyocyaneus.* Repeated examinations for tubercle bacilli were negative, as were several inoculations into guinea-pigs.

Examination of the blood on Nov. 23, 1927, showed: red blood cells, 3,350,000; leukocytes, 14,400; hemoglobin, 30 per cent; neutrophils, 58; small mononuclears, 38, and transitionals, 7. Subsequent examination of the blood demonstrated a gradual increase in the leukocyte count. On December 1, there was a leukocytosis of 38,200. The blood pressure was systolic, 110; diastolic, 80. The Pirquet test was negative. The blood chemical determination on Nov. 26, 1927, showed a total nonprotein nitrogen of 54.5. Only a faint trace of phenolsulphonphthalein was detected at the end of five and one-half hours.

Under ethylene anesthesia, soft rubber catheters, nos. 10 and 12, could not be passed. It was impossible to introduce the cystoscope because of an obstruction apparently in the prostatic urethra. Finally, after much manipulation a small soft rubber catheter was passed and a cystogram was made. A regurgitation of fluid up the left ureter and into the left kidney pelvis causing an enormous dilatation of the pelvis and ureter could be clearly outlined. The ureter was markedly tortuous. The outline of the pelvis extended from the twelfth dorsal to the first sacral vertebra. There was some dilatation of the lower end of the right ureter (fig. 1).

On roentgen examination, the chest showed some elevation of the diaphragm, especially of the right side. The heart was a little transverse in position, and its contour unusually rounded. Moderate intensification of the markings in each lung field and a little flaky increase from the right hilum for a short distance were found. The field of the lower lobe of the left lung was unusually clear. On roentgen examination of the genito-urinary tract, a stone was not found.

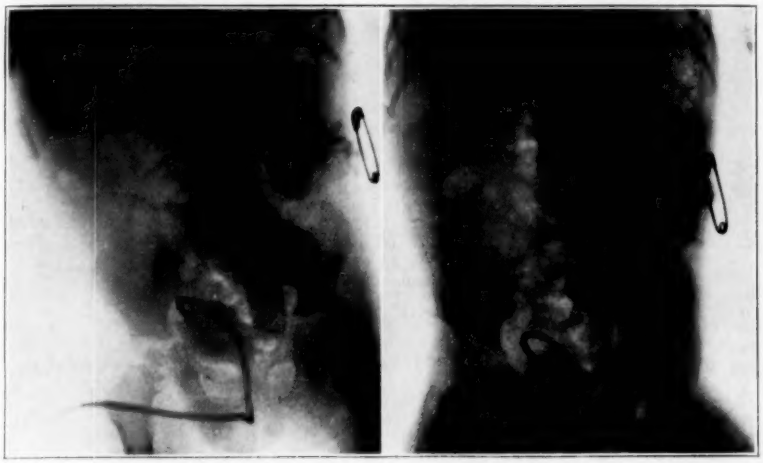
Operation.—On Nov. 26, 1927, operation was performed under ethylene and ether anesthesia. Because of the presence of an enormous swelling in the left renal area, the severe degree of infection in the urinary tract and the high temperature, it was decided to operate on the left kidney for the purpose of drainage only.

The usual oblique incision was made in the kidney. Blood escaping from the vessels was pale and watery. The kidney was lobulated and dilated and had large

hydronephrotic sacs filled with purulent fluid. In the renal cortex were multiple abscesses which varied in size from that of a split pea to that of a dime. The distended kidney was aspirated with a syringe. The fluid contained 18,720 pus cells per cubic millimeter, and the cultures showed *Bacillus pyocyaneus*. The aspirating syringe was withdrawn, the opening enlarged, and a rubber tube inserted into the kidney.

Following the operation there was some definite improvement, and because of this it was decided to attempt again to overcome the urethral obstruction in the hope of using the cystoscope. On December 5, bougies ranging in size up to and including no. 14 were passed, and finally a soft rubber catheter was introduced.

Cystoscopic Examination.—On December 20, examination revealed a trabeculated bladder and normal ureteral orifices. In the right ureteral orifice, a large flake of thick pus was noted.



A B

FIG. 1 (case 2).—Cystogram showing the enormous dilatation and tortuosity of the left ureter as well as the presence of a large hydronephrosis.

In view of the fact that the left kidney was the seat of advanced disease and because of the improvement of the child following nephrostomy, the advisability of nephrectomy was discussed. The removal of the diseased kidney was, without doubt, the proper procedure. Moreover, at the time cystoscopy was done, it was impossible to catheterize the right ureter.

Second Operation.—On December 12, operation was performed. Since a pyelogram could not be made because of an obstruction to the advancement of the catheter, a surgical exploration was advised. Exploration of the right kidney showed exactly the same change that had been found in the left kidney, namely, a large kidney extending high under the ribs and low into the iliac fossa. The kidney seemed to contain only a moderate amount of renal tissue which had undergone hydronephrotic changes. There was no sign of any cortical abscesses. Cloudy urine was obtained by aspiration.

Following the operation, the patient gradually became weaker and died on Jan. 9, 1928.

Autopsy.—On the same day, autopsy was performed by Dr. Carl Apfelbach, pathologist of the Presbyterian Hospital. The body weighed 18½ pounds (8.4 Kg.). There was no free fluid in the peritoneal cavity. The urinary bladder extended up to within 4 cm. of the umbilicus. At its upper end, there was a fluctuant mass about 4 cm. in diameter. The ureters on both sides were markedly tortuous and dilated, so that in most of their extent they were from 3 to 4 cm. in circumference. The openings into the urinary bladder were only 9 or 10 mm. in circumference. The colliculus seminalis was only 2 mm. in its largest diameter. The prostatic portion of the urethra was asymmetrical, because on the right side there was a shallow pouch marked off distally by a thin fold of mucous membrane 1 cm. long. The left half of the urethra was only about 4 mm. from front to back, and the mucous membrane here was folded. The renal pelves on both sides were dilated to a circumference of about 10 cm. at the inferior major calix. The calices were distended, and the medullary portion was sparse. Multiple abscesses and regions of necrosis were found in the cortex of each kidney. *B. pyocyaneus* and *Staphylococcus aureus* were isolated from the abscess outside of the upper end of the urinary bladder.

The cause of death was ascending cysto-ureteropyelonephritis subsequent to congenital hydronephrosis and hydro-ureter due to a congenital valve in the prostatic portion of the urethra (fig. 2).

CASE 3.—*History.*—R. C., a boy, aged 1 month, was admitted to the Children's Memorial Hospital, Sept. 12, 1927, with a complaint of projectile vomiting. The specimen was given to us for study by Dr. J. A. Bigler, resident pathologist at the Children's Memorial Hospital. The child was born on Aug. 12, 1927, and was breast fed until September 3, at which time he was put on a milk and water formula. He continued to vomit, and several different feeding formulas were tried without success. The child continued to lose weight, and the night before he was admitted to the hospital he had a convulsion. There were no urologic symptoms of any kind.

Examination.—The infant was markedly dehydrated, and projectile vomiting occurred. The results of the examination were negative except for a slight injection of the throat and a questionable mass, the size of a walnut, in the right upper epigastrium. Peristaltic waves were visible.

After due consultation, a diagnosis was made of a pyloric obstruction and operation was advised.

Operation.—The operation was carried out on Sept. 12, 1927, but no pyloric tumor was found. The kidneys and ureters were not examined, and the abdomen was closed. The temperature varied from 100 to 102 F. during the stay in the hospital.

The child died on the second day following the operation.

Autopsy.—Bilateral hydronephrosis, ureteritis and considerable pus in the urine with positive cultures of streptococci and *B. coli* were found. A slight bronchopneumonia was present. Both kidneys were moderately hydronephrotic. The ureters were markedly dilated and tortuous. The bladder wall was thin, almost like parchment. No trabeculations, diverticula or stones were found. A cleft verumontanum, of moderately enlarged dimensions was seen in the prostatic urethra. Running toward the bladder were two mucous folds extending from the clefts of the verumontanum to the lateral walls of the prostatic urethra, one on each side. They were so constructed and situated as to form a bicuspid valve tending to obstruct urinary outflow, their concavity facing toward the bladder. The obstruction was not quite complete (fig. 3).

LITERATURE

Some of the early literature on the subject of posterior urethral obstruction was confusing in that no clear distinction was made between valves, strictures, stenoses and inflammatory conditions.

Velpeau, in 1851, in speaking of fibers on the lower segment of the vesical extremity of the urethra, said that these constitute a sort of

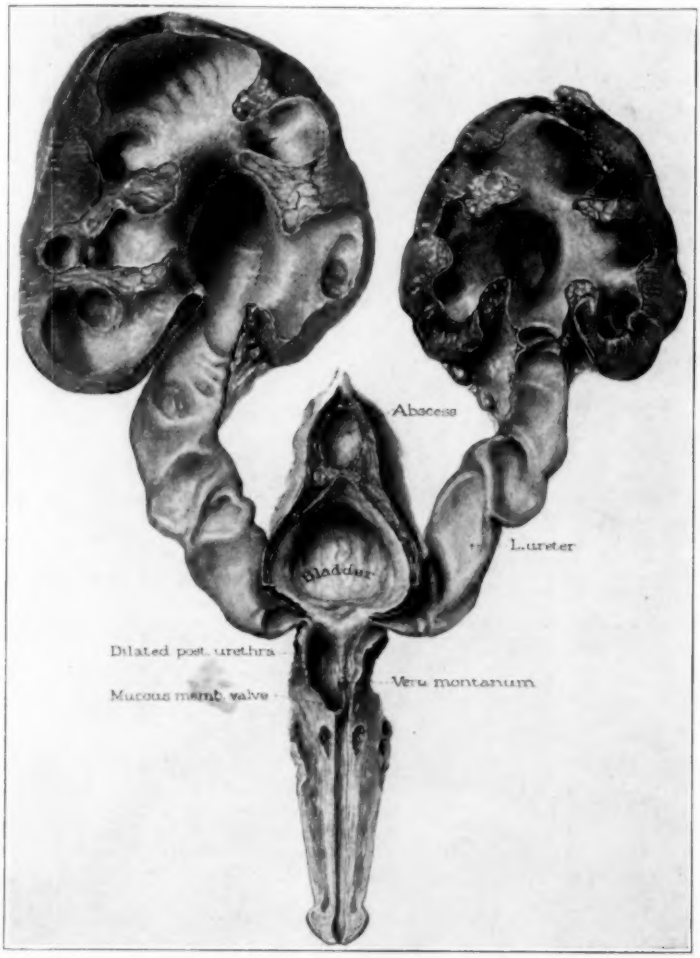


FIG. 2 (case 2).—Valve in the urethra behind which the urethra is dilated. Enormous dilatation of the ureters and kidney with the presence of normal ureteral openings.

half sphincter which, in case of organic contraction in some part of the passage, is apt to become inflamed and irritated to such a degree that the resulting contraction forms a valve which momentarily closes up this orifice and prevents the escape of urine until the contraction passes, through fatigue, into relaxation. It should be added that this

is not an example of a congenital valve; nevertheless, Velpeau has been given credit by many modern writers for being one of the first to mention the condition.

Among the earliest cases in the literature are those of the following writers: Budd, in 1840, reported a case in a sailor, aged 16, who died several days after admission to the hospital in a state of coma. Godart, in 1854, compared the valves in his case to a pigeon's nest or the sigmoid valves. Picard, in 1855, described a case of true valves

FIG. 3 (case 3).—Dilatation of the kidneys and ureters and the presence of a valve of the posterior urethra. *A* shows the "wings" of the verumontanum obstructing the ureter.

complicated with convulsions. Autopsies were performed in all of these cases; hence, the diagnoses were not mere speculation as they are in many instances.

In 1870, Tolmatschew wrote the first discussion with regard to congenital valves of the posterior urethra as a definite clinical entity and brought the literature up to date, describing the cases of Budd, Bednar, Godart and Guyons.

Young, Frontz and Baldwin, in 1919, reported twenty-three cases found in the literature and added reports of twelve of their own cases.

In 1925, Hinman and Kutzman added six personal cases and fifteen additional cases in the literature, making a total of fifty-six. A thorough search of the literature since Hinman's summary in 1925 reveals eight more cases and the addition of three of our cases makes a total of sixty-seven reported to date.

TYPES

In reviewing the literature, Tolmatschew found references to several classifications, such as Jarjavay's description of circular and semilunar valves, and Bouillard's mention of the possibility of twofold and threefold valves. Then he stated that the known valves have been divided into four classes, namely: (1) those posterior to the fossa navicularis; (2) those posterior to the bulbous urethra; (3) those anterior to the verumontanum, and (4) at the anterior margin of the field in front of (3).

Modern writers classify their cases according to the system of Young, Frontz and Baldwin, which consists of three types: 1. One or two semilunar folds running anteriorly from the verumontanum toward the penile urethra. 2. Semilunar folds running posteriorly from the upper edge of the verumontanum. They describe only one case of this type, in which a valve consisted of two folds. 3. The iris valve, bearing no relation to the verumontanum and attached to the entire circumference of the urethra, with a small opening near the center.

PATHOLOGY

The same anatomic changes are produced by all such valves and are similar to the changes produced by obstructions of the neck of the bladder. There is an early compensatory hypertrophy and later on dilatation of the bladder which finally extends to the ureters. This process is usually present in both ureters but in differing degrees. Randall reported a case in which there was a true unilateral hydro-ureter. Some patients with large patent ureterovesical orifices have been found with small bladders. If this condition is allowed to progress hydronephrosis results on both sides, and infection invariably sets in. One of our cases showed a perivesical urinary abscess at the fundus of the bladder. This is not a common occurrence.

ETIOLOGY

The etiology of congenital valves of the deep urethra is not known; hence, several theories have been elucidated in an attempt to explain their formation. Most of these theories are due to the fact that a writer has been interested only in one type, and of course it stands to reason that one theory will not explain all three types of valves.

Tolmatschew believed them to be the result of overdevelopment of folds normally present in the urethral mucosa, as described in "Anatomy of Man" by Luschka. Later writers who have agreed with him are Wilckens and Knox and Sprunt. The latter writers said: "The folds or valve-like obstructions in which we have been most interested seem to occur in those regions where folds and ridges are normally found in the urethral mucosa, and this is especially true of the anterior end of the colliculus seminalis where most of these obstructions are encountered. Here in the normal urethra there is a division of the crista urethralis into two ridges which, becoming less and less prominent, gradually fade out in the posterior wall of the bulbous urethra. In most of the reported cases of obstruction at this point, the lesion seems to have been produced by an overdevelopment of these folds which fuse with the anterior wall with the formation of membranes extending across the urethral lumen. In the lack of definite knowledge we lean rather to the view that we are dealing with a simple progressive malformation and not one due to arrest of development."

Young, Frontz and Baldwin stated that "the anatomical view advanced by Tolmatschew may explain the semilunar form but not the iris type of valve." With regard to the presence of normal folds in the mucosa, Gray stated: "In the cavernous and membranous portions the mucous membrane is arranged in longitudinal folds when the tube is empty." No mention is made of folds in the prostatic urethra.

F. P. Johnson asserted that: "On the anterior and lateral walls of the prostatic urethra smaller and less constant longitudinal folds are found."

Writers who were interested chiefly in the type 3 valve have laid emphasis on the theory that such structures are the result of persistence of a portion of the urogenital diaphragm. The rôle of this diaphragm has been clearly described by Keibel and Mall, whose thesis was quoted by Nicholson in describing the development of this organ. Bazy based his case on this theory, as did Thompson, who stated: "Presumably this septum must be the structure formed by the meeting of the cloacal hypoblast and the invaginating perineal epiblast analogous to the anal and hymenal membranes." Lederer also believed this theory, and Young, Frontz and Baldwin stated that, "the embryological explanation suggested by Bazy appeals to us as very probably accounting for the occurrence of the semicircular diaphragms, which are attached to the urethra throughout half of its circumference and the iris-like variety of Jarjavay."

In speaking of strictures and valves, Mixter said: "Stricture occurs where the downward growing proximal urethra and the inward growing distal segment fail to unite accurately." Two patients have been seen in whom the two segments ended blindly and communication occurred

through a minute lateral opening where the blind ends overlapped. Valves are formed by folds of mucous membrane that usually arise close to the verumontanum and are attached to the circumference of the urethra below the internal vesical orifice. Lewis said, "it is interesting in this connection to remember that an epithelial concrescence occurs in the development of certain organs. Such a concrescence or persistence of parts of the urogenital membrane may account for some of these urethral clefts." Lowsley stated that he did not believe valves to be the result of remnants of the urogenital membrane, since "it is difficult to explain why this particular anomaly should occur so frequently, as the point of obstruction in this and similar cases is above the junction of the pars membranacea and the pars bulbosa, which is the generally accepted point of division between that part of the urethra which develops from the entoderm and that which is derived from the ectoderm." However, in his case the valve was of type 1, which no author has attempted to explain by this theory. Only type 3 can be the result of the urogenital membrane.

A third theory was advanced by Lowsley. He stated that "this case seems to be an anomaly of the Wolffian and Müllerian ducts rather than a defect of the urethra itself. These structures which in the male become the ejaculatory ducts and the utriculus prostaticus enter the prostate near the base and course in an oblique direction through that organ until they approach the urethra, at which point they turn and for a short distance run parallel with its axis, finally opening into its lumen. During their passage through the prostate, their musculature is bound together by a very definite firm sheath of connective tissue. On their approach to the urethra, they push the floor of that structure up into a mound, forming the verumontanum and still are separate from all other structures, their tissues being superimposed upon those of the urethra. Ordinarily, immediately below the openings of the ejaculatory ducts and utricle the tissues surrounding them become distributed among the fibers on the floor of the urethra. Thus the verumontanum gradually becomes smaller and smaller until just below the apex of the prostate it disappears completely, spreading out laterally in the form of little bands which disappear in the floor or walls of the urethra. In the specimen under consideration, although a number of fibers are disposed in the usual manner the majority of them continue downward on the floor of the urethra. At the point where the verumontanum usually disappears, these fibers attach themselves to the entire circumference of the urethra with the exception of a small portion of the floor to the left of the median line, thus causing an almost complete blocking of the urinary passage."

A fourth possible explanation for the occurrence of valves was mentioned by Young in his discussion of Watson's work on the structure

of the verumontanum. Watson made sections of the verumontanum in various stages of fetal life. One of these, from a 16 week's old fetus, happened to show three fibrous strands arising from the summit of the verumontanum and attached to the roof of the urethra. Young said that "it seems highly probable that this anomaly represents an early stage of valvular obstruction." He also added that "this anomaly, however, seems wholly inadequate in accounting for the origin of the valve-like obstruction at the vesical neck which arises from bifurcation of the ridge which springs from the upper aspect of the verumontanum, as well as the semicircular folds in the roof or the floor which may occur at any level."

This leaves only type 1 to be accounted for by these fibrous strands. A similar explanation was adopted by Hinman from a theory proposed by Professor Fischl of the University of Vienna. Hinman stated that "a proliferation of the epithelium of the roof of the sinus urogenitalis with subsequent connective tissue adherence to the opposite wall can account for the anomaly. Such a process with the required variations in the different places can explain not only such anomalies as bridges and bands that act like a diaphragm but also the more common valves as well as structures."

After reviewing the various theories, it can readily be seen that one theory cannot explain all types of valves.

Type 1, or the folds from the lower end of the verumontanum toward the penile urethra, is probably formed in one of two ways: 1. If there is overdevelopment of normal urethral folds, they would be ballooned downward by urinary pressure. Lowsley's theory of an anomaly of the wolffian or müllerian ducts would come under this group.

2. If fibrous tissue strands between the roof of the urethra and top of the verumontanum were large and offered any degree of hindrance to urinary outflow, they would be ballooned in the direction of the urinary current.

Type 2 valves could be the result of similar strands only if they were small and offered no resistance to urinary outflow until later. As the urethra increases in length, the verumontanum is probably carried peripherally to a greater extent than the roof of the urethra because of the greater prostatic development in the former location. Therefore, the longitudinal folds would be drawn into the form of type 2 valves.

Type 3 valves are, no doubt, the result of the persistence of remnants of the urogenital membrane. It is interesting to observe the great diversity of opinion as to the embryology of the urethra, the majority of writers agreeing on the entodermal origin of the prostatic urethra and the ectodermal origin of the anterior urethra, the two parts uniting at the urogenital membrane. This was described by Bailey and Miller. On the other hand, Nicholson said, "it would seem that the urethra

must be entirely composed of entoderm." Therefore, until the exact mechanism of the embryologic formation in the region of the urethra and the deviations from its normal are understood, one cannot hope to know the cause of these valves.

SYMPTOMS

For a varying period of time, cases of this type may run a more or less silent course; often the onset of the symptoms is ushered in with a chill due to the onset of infection. As a general statement, one may say that the symptoms may be divided into three groups: those due to obstruction, those due to infections and general symptoms.

Those Due to Obstruction.—Symptoms due to obstruction in the infant do not differ from those in the adult. As a rule, the symptoms begin early in life. In the three cases reported in this paper, the symptoms in one began at the age of about 19 months and in the other two cases, they dated from birth. A history of symptoms suggesting obstruction at the bladder or in front of it should always arouse one's suspicions of the possibility of valves in the deep urethra. These symptoms are similar to those in the adult with obstruction; thus, dribbling is constantly present as well as difficulty in starting the stream and a small stream. Straining and hesitation are not uncommon, and occasionally the mother states that the child can micturate better in one position than in another. Cases are recorded in which the urine comes out drop by drop. Locally, the presence of a suprapubic tumor due to the full bladder often gives the clue to the real situation.

Those Due to Infection.—Symptoms due to infection may be the first manifestations of disease in the urinary tract. The patient is suddenly seized with severe chills, and these are followed by a sharp rise in temperature after which profuse sweating occurs. The frequent occurrence of chills and fever with pus in the urine often leads to a diagnosis of pyelitis, especially when these attacks recur.

General Symptoms.—General symptoms occur with the second group of symptoms, or at times they may predominate in the picture. Anorexia, nausea and vomiting may so completely overshadow the urinary symptoms that the case may be looked on as one of gastro-intestinal disturbance. Indeed, in one of the cases in this series, the patient was operated on for pyloric stenosis. This may be particularly apt to occur in very young children in whom the urinary symptoms are not carefully noted by the mother.

DIAGNOSIS

The History.—Of equal importance is the history. There is always some history of urinary distress, as previously mentioned, only one must take pains to elicit it. Besides the history of urinary symptoms

is that of duration and onset, that is, whether the symptoms began shortly after birth or early in life. These symptoms and their onset gradually get worse; at best, there is a history of only a slight remission of the symptoms.

Suprapubic Tumor.—A suprapubic tumor can generally be demonstrated by both inspection and percussion and, naturally, the older the child the larger and more pronounced the tumor.

Instrumental Examination.—Next in establishing a diagnosis is the instrumental examination. There may or may not be obstruction to the passage of a catheter or a cystoscope. In our first case I had difficulty in the passage of a small soft rubber catheter so that a preliminary dilatation with bougies was necessary before cystoscopic examination was possible. This instrumental examination shows the presence and amount of residual urine, which is a constant observation. When residual urine is found in these young children, three lesions should immediately be considered: (1) contracted neck of the bladder; (2) disease of the central nervous system, and (3) congenital valves of the urethra.

Cystogram.—Cystographic examination can be carried out at this time and gives one a good idea of the extent of damage that has been done to the kidneys and ureters. The results of these examinations are often great surprises in showing far advanced dilatation of the kidneys and ureters when least suspected.

TREATMENT

The treatment may be divided into surgical and nonsurgical. The surgical procedure consists of a suprapubic cystotomy and the destruction of the valve. Frontz has advised the nonsurgical treatment by means of an especially small constructed Young punch. Needless to say, before any form of treatment is carried out careful study of the function of the kidney should be done just as it is in the adult with obstruction.

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INTESTINAL PNEUMATOSIS *

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Intestinal pneumatosis is a rare condition characterized by the presence of gas in endothelial-lined spaces in the intestinal wall and by a chronic productive inflammation in the surrounding tissue. Turnure [1] and Mills [2] have reviewed the literature, the latter collecting the reports of 100 cases. In only one of these did the disease occur in an infant; this was in a case reported by Maass.[3] During the past three years I have encountered four cases in children at the Babies and Childrens Hospital. This incidence of four cases in 260 autopsies convinces me that the disease in infants is more frequent than has been supposed.

REPORT OF CASES

CASE 1.—A white girl, aged 9 weeks, was admitted to the hospital with a history of convulsions of four hours' duration. Examination revealed dehydration, respiratory difficulty and clonic spasm of the face and extremities. Diarrhea had existed for two days, but there was no vomiting. Death occurred forty-eight hours after admission without unusual symptoms other than a profuse hematemesis immediately before death.

Autopsy seventeen hours after death revealed a diffuse hemorrhagic enteritis, acute mesenteric lymphadenitis, intestinal pneumatosis, edema and pneumonia of the upper lobe of the right lung and hyperplasia of the thymus.

The stomach contained 50 cc. of coffee-ground material, but was otherwise normal. The entire small intestine was markedly hyperemic, with many small mucosal and submucosal hemorrhages. Over many of these hemorrhages the mucous membrane was eroded. Peyer's patches were slightly hyperplastic. The intestinal contents were fluid and dark red. Throughout the jejunum and ileum, in the mucosa and submucosa, were many small gas bubbles, varying from a minute size to a diameter of 3 mm. The mucosa of the colon was hyperemic and showed a few small petechiae. The solitary follicles were enlarged and hyperemic.

Microscopically, the gas was confined to definite spaces, lined in part by flat, endothelial-like cells and located largely in the submucosa but extending into the

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2. Mills, H. W.: Gas Cysts of the Intestine with Report of Three Cases, Surg. Gynec. Obst. **40**:387, 1925.

3. Maass, H.: Demonstration eines Präparates von Emphysem des grossen Netzes, Berl. klin. Wchnschr. **41**:401, 1904.

mucosa and serosa. About many cysts the tissue was edematous and hyperemic and was infiltrated with mononuclear wandering cells and extravasated red cells. No giant cells were present. The submucosa contained an increased number of fibroblasts and young blood vessels. The mucosa was the seat of an intense acute hemorrhagic inflammation. The lymph nodes about the intestine were hyperplastic, with lymphangiectasis of their peripheral sinusoids (fig. 1).

CASE 2.—A white girl, aged 14 months, was admitted to the hospital with a history of vomiting from ten to twelve times a day for three days and marked diarrhea. Death occurred on the third day without notable alleviation of symptoms.

Autopsy eight hours after death revealed an acute catarrhal entercolitis, acute hyperplastic mesenteric lymphadenitis, intestinal pneumatosis, hyperemia, edema, atelectasis and acute emphysema of the lungs, fatty metamorphosis of the liver,

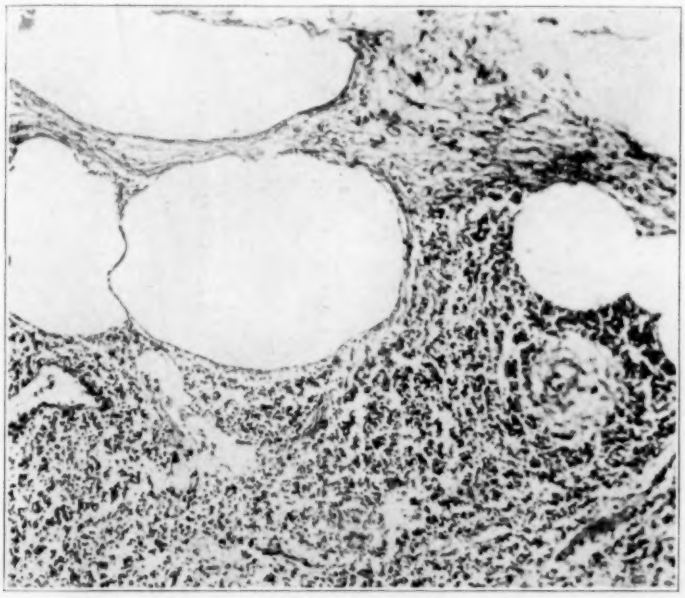

Fig. 1 (case 1).—Dilatation of the peripheral sinusoids of a mesenteric node; × 90.

cloudy swelling of the kidney, passive hyperemia of the spleen and acute suppurative mastoiditis on the right side.

The stomach was normal. The mucosa of the jejunum and ileum, especially the terminal ileum, was swollen and hyperemic and showed many petechiae. The lymphatic tissue was hyperplastic. There were no gross ulcerations. Throughout the small and large intestine, there were many gas bubbles, varying from 0.5 to 2 mm. in diameter in the submucosa. The cysts were most abundant in the ascending colon and were associated with a hyperemic, swollen, soft mucous membrane.

Microscopically, the cysts, confined to the mucosa and submucosa, were lined by a flat, endothelial-like cell with an occasional giant cell in the wall. A few of the cysts were surrounded by a collar of lymphoid tissue. The surrounding fibrotic submucosa contained only an occasional wandering cell. The mucosa was the seat of an acute catarrhal inflammation.

CASE 3.—A white boy, aged 6 weeks, was admitted to the hospital because of failure to gain weight and an acute otitis media. Vomiting, often projectile, had occurred from one to four times a day for five weeks previous to admission. Death occurred on the fourteenth day in the hospital.

Autopsy seventeen hours after death revealed an acute hemorrhagic enteritis, acute mesenteric hyperplastic lymphadenitis, intestinal pneumatosis, bilateral acute suppurative otitis media and mastoiditis, hyperemia and edema of the brain, congestion, edema, atelectasis and acute emphysema of the lungs, fatty metamor-

Fig. 2 (case 3).—Section through the septums between two cysts. Note the circular fibrin deposits, the cellular infiltration, edema and vascularization of the tissue; × 245.

phosis of the liver, cloudy swelling of the parenchymatous viscera and healing rickets.

The stomach was contracted, the mucous membrane covered by a thick viscid mucus; otherwise there was no abnormality. The small intestine was dilated by gas. The mucous membrane of the jejunum was hyperemic and covered by a thin seromucinous exudate. In the terminal ileum, the exudate was fibrinous and moderately adherent. In the ileum, 15 cm. above the ileocecal valve was an ulcer, 5 mm. in diameter, irregular in outline and not indurated. The

lymphatic tissue of the ileum was hyperplastic. Throughout the submucosa of the jejunum and iluem were many gas bubbles, varying from 0.5 to 2 mm. in diameter and arranged in groups of from eight to ten. The colon was normal except for slight hyperemia of its mucous membrane.

Microscopically, the serosa was edematous and hyperemic and contained a few small cystic spaces. The muscularis was normal. Throughout the submucosa were spaces lined in part by flat, endothelial-like cells with an occasional giant cell. In the wall of many smaller cysts were deposits of fibrin (fig. 2). The surrounding tissue was edematous and highly vascularized and was infiltrated with mononuclear cells. The mucosa was the seat of an acute catarrhal inflammation.

CASE 4.—A white girl, aged 2 weeks, was admitted to the hospital because of a diarrhea of one week's duration and a skin eruption. Death occurred on the seventh hospital day without notable alleviation of the symptoms.

Autopsy four hours after death revealed an acute catarrhal enteritis, intestinal pneumatosis, pemphigus and patent foramen ovale.

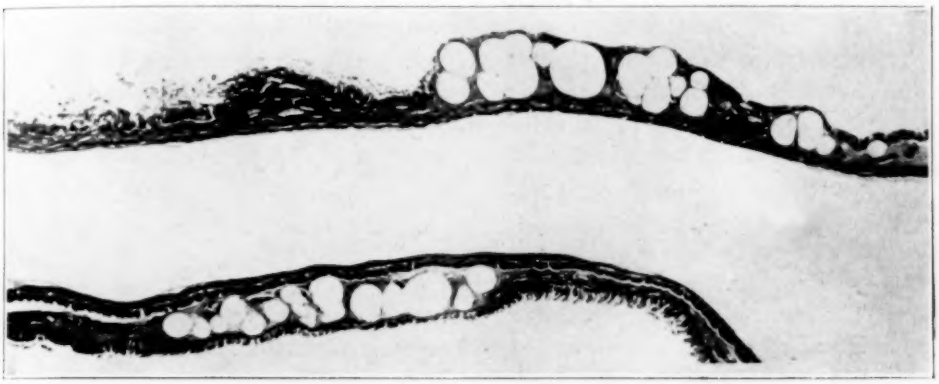

Fig. 3 (case 3).—Two sections of small intestine to show the general appearance; reduced from a magnification of × 9.

The stomach was normal. The small intestine was normal, except the terminal ileum, in which the mucous membrane was hyperemic and swollen and covered by a light yellow, viscid, sticky exudate. The mucous membrane of the large intestine was swollen and hyperemic but not ulcerated. Throughout the colon, in the mucosa and submucosa, were groups of gas bubbles, varying in size from 0.5 to 1 mm.

Microscopically, the cysts were found largely in the submucosa and mucosa with an occasional small cyst in the serosa. The histologic features were similar to those in case 3.

MacCallum stains for bacteria were negative in all four cases.

PATHOLOGIC FEATURES

The disease in infants, as seen in these four cases, differs in certain respects from the published descriptions of the disease in adults. In infants the dominant location of the cysts is the mucosa and submucosa with few in the serosa, while in adults the serosa is predominantly

involved. Microscopically, giant cells have been described as the prominent feature in adults. In my cases giant cells were inconspicuous and were observed only in the smaller cysts in association with fibrosis and fibrin deposits.

In general in these four cases the cysts were confined to either the small or the large intestine. The cysts were, as a rule, grouped in small islands of from six to eight distinct bubbles and were not diffusely distributed. They were freely movable from one point to another through the wall. The muscularis was seldom involved.

Microscopically, the tissue about the cysts was the seat of a chronic productive inflammation. There was an increase of fibrous tissue, marked vascularization and slight to moderate infiltration of mononuclear wandering cells. The cysts were lined by flat cells resembling endothelium. In rare instances similar spaces were present in the lymph nodes contiguous to the intestine. Giant cells about the cysts in infants are apparently rare. In the wall of some of the smaller cysts there are fibrin deposits. These deposits are associated with fibrosis and cellular infiltration and are most extensive in small cysts.

Bacteria, identified by culture or staining, have been reported, but in my four cases and in that of Sloan [4] from this laboratory none were present in the tissues.

THEORIES OF ORIGIN OF THE GAS

Four theories have been proposed to explain the origin of the gas. The mechanical theory postulates that the gas enters from the intestinal lumen through a small gross or microscopic ulceration. The bacterial theory hypothecates that the gas is the result of bacterial action. The neoplastic theory considers that the cells lining the cyst are neoplastic and have acquired the property of gas formation. The chemical theory proposes that certain cells, not neoplastic, have gained the capacity to form gas by specific protoplasmic action.

Any theory must conform to the known general principles of pathologic processes. That cells in other diseases do not acquire the capacity of forming gas is a powerful argument against the chemical theory. In fishes certain specialized cells have the property of excreting oxygen, and pneumatosis has been compared to this. The few chemical analyses [5] of the gas which have been made, reveal a mixed gas, containing carbon dioxide, oxygen, hydrogen and nitrogen; hence the process is not analogous to the swim bladder.

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5. Urban, K.: Ueber Pneumatosis Cystoides Intestinorum, Wien. med. Wchnschr. **60**:1750, 1910.

The neoplastic conception is inconsistent with the microscopic picture. None of the cases exhibits the usual characteristics of a neoplasm. Many cases in which there was spontaneous cure with microscopic evidence of healing are extant. Finally, no known tumor is associated with the production of gas by the tumor cell.

The bacterial theory rests on the identification of bacteria in the tissue. In my cases and in many others in the literature bacteria have not been demonstrated. In other bacterial emphysematous diseases bacteria are present in large numbers. The evidence of productive inflammation about the cysts eliminates postmortem production of gas by bacteria.

The evidence for the mechanical theory is strong. The majority of cases are associated with some lesion inducing hyperperistalsis, such as gastric ulcer, pyloric stenosis or an enteritis. In many cases there is gross ulceration of the gastro-intestinal tract and in others, associated diseases in which microscopic breaks in the mucosa are frequent. The absence of bacteria supports the mechanical theory as strongly as it belittles the bacterial theory.

SUMMARY

Four cases of intestinal pneumatosis in infants are reported.

The pathologic picture is the presence of gas in endothelial lined cysts of the intestinal wall with a chronic productive inflammation in the surrounding tissue.

The gas is derived from the intestinal lumen and enters the wall by a mechanical process through an ulceration in the mucosa.

Dr. Howard T. Karsner aided in the preparation of this paper and of the accompanying photomicrographs, Dr. H. J. Gerstenberger provided the clinical material and Dr. Harry Goldblatt the pathologic data for cases 1 and 2.

Progress in Pediatrics

MENTAL HYGIENE FROM A PEDIATRIC STANDPOINT

A STUDY OF FOUR HUNDRED CASES IN A PRESCHOOL CLINIC*

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The Minneapolis Infant Welfare Society was organized in 1910. A special department for preschool children was inaugurated ten years later. From the beginning, in the preschool clinics the child was viewed not merely from the physical, but also, and especially, from the mental and emotional side, with the hope of proving that many of the behavior problems in children can be prevented by early training.

As a result of eight years of experience, habit training was gradually extended to the infant clinics. As a corollary, the upper age limits of infants were increased to 3 and then to 4 years. A "progress chart" of the infant's mental development and habit formation is kept from the twelfth month to the fourth year; if any difficult problem arises, the case is turned over to the preschool department for more intensive study. On the diet card for each month are presented suggestions for the habit training of the child which are to be emphasized at the various ages. For example, on the diet card for the sixth month appears: "Each new food is given in small amounts at first. The baby may refuse this. He does not refuse food because he does not like it. Be firm and persistent. If he spits it out give him another mouthful. The holding of breath in a tiny baby is one form of a tantrum. Parents should remember that the baby cannot hurt himself by crying." On the diet card for the eighteenth month there is the following: "Parents should remember to talk slowly and distinctly and avoid all baby talk. A child learns to talk through imitation."

In the preschool clinic itself 70 per cent of the children are referred from the infant department; the remainder come on the recommendation of the mothers through various forms of publicity or they are referred by other agencies. The city is divided into seven districts, in which nine clinics a month are given. The nursing staff consists of a supervisor and four nurses. These nurses are all graduates of a public health training course and have had special instruction in child training. The clinics are conducted by the medical director and two other staff

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physicians, all of whom are pediatricians especially interested in child psychology. Rather than to have separate "habit clinics" and clinics for the consideration of physical defects, it was felt that a pediatrician with a sufficiently broad outlook could better coordinate the various aspects of the problem and consider the child as a whole. The pediatrician rather than the psychiatrist is the one who sees the problem cases at the beginning, when a little practical advice to an overanxious mother or a restraining influence on a too severe father may nip the potential problem at its inception. If the problem in the case presents unusual difficulties, the child is referred to the Child Guidance Clinic of the Minneapolis Public Schools.

The service consists of individual consultation with the physician at the clinic and intensive follow-up work in the homes, the frequency of

TABLE 1.—*Reason for Attending Clinic*

Reason	Number of Cases
General advice	199
Feeding problem	92
Weight (thinness or loss)	63
Tonsils and adenoids	49
Enuresis	31
Control (tantrums, training, nervousness, irritability)	30
Frequent colds	30
Stomach condition	20
Constipation	15
Suspected worms	13
Glands	8
General physical	6
Night terrors	5
Teeth and gums	5
Speech defect	4
Sleep	2
Poor "mixer"	2
Miscellaneous (rickets, conditions of the heart, skin and kidneys, hernia, earache, fatigue, headache, pain and other condtions, thirty-three in all)	66

the home visits depending on the case. Physical defects are corrected, adequate diets secured and behavior problems considered. An intelligence test for each child has been made possible through the cooperation of the Department of Psychology of the University of Minnesota. The cooperation of both parents is sought and every attempt is made to produce a suitable environment. The children are encouraged to play with others of the same age. Whenever possible the children are sent to nursery schools, where the problem often disappears automatically. Exceptionally difficult cases are sometimes temporarily "boarded out." A pamphlet, "Your Child," and Dr. Thom's book, "Child Management," are given to the parents. Books relating to the management of children are loaned from the clinic library. Among others, Cameron's "The Nervous Child," Thom's "Everyday Problems of the Everyday Child" and Blanton's "Child Guidance" are popular.

To obtain a cross-section of the work, 400 consecutive cases were analyzed. Table 1 gives the reasons for attending clinic. Except for

the cases brought in on account of poor control, speech defect, poor "mixing" and night terrors, a total of forty-one, all the others were presented for purely physical conditions. Tables 2 and 3 give a picture of what was actually found in the clinic. Table 2, presenting the conditioning factors, shows that outside of 137 physical conditions the majority of factors resided in the parents or environment, a potent argument for parental education. This table especially shows the interrelation between the physical and emotional causes. Many of the children with physical defects had emotional strain and poor understanding as a conditioning factor. In other cases the relative importance of the two was reversed, the physical factor being a relatively minor one. Thus it can be seen how difficult it is to separate the physical side and

TABLE 2.—*Conditioning Factors in Parents or Environment and in the Child*

	Number of Cases
In the Parents or Environment	
Lack of understanding	217
Lack of firmness	213
Poverty and sequences	86
Poor health	76
Too litttle outdoors	76
No playmates	51
Too much attention	22
Lack of agreement	31
Emotional strain	25
Lack of attention	19
Mental defect	16
Too rigid discipline	14
Grandmother	10
Foreign	2
In the Child	
Physical condition	137
Mental defect	9
Poor "mixer"	8
Mental superiority	6
After-effects of disease or injury	6

habit side of the child's life. Practically all the children were brought to the clinic because the parents felt that there was a physical basis for their ills. If the physician conducting the clinic was not "psychologically-minded," he could easily overlook most of the habit problems involved; even though he had a habit clinic to which to refer them, he would frequently be unable to recognize the habit problem when he encountered it. In fine, both in clinics and in private practice, "habit" cases are brought to the physician as instances of physical defect, and he must be educated to recognize the emotional factors involved and be prepared to give advice and treatment in the simpler cases.

Table 3 classifies the defects discovered. Here again, aside from frequent colds, tonsils and adenoids, teeth, constipation and poor condition, the other aspects involve directly or indirectly poor parental management. The basis for advising tonsillectomy and adenoidectomy was not so much the appearance of the tonsils, as the history of frequent colds and infections and their effect on the physical condition of

the child. In other words, the history of the case and a consideration of the child as a whole were thought to be more important factors in the decision than the local condition of the nose and throat.

Table 4 gives the number of defects per child. The greatest number of cases showed from one to six defects, both physical and emotional.

TABLE 3.—*Conditioning Factors Recognized in This Study*

Underweight (7 per cent or more)	133
Poor condition (from physician's dictation)	31
Poor diet	156
Inadequate diet	125
Constipation	80
Enuresis	94
Less than eleven hours' sleep	55
No nap	178
Poor parental control	201
"Night terrors" and excessive restlessness	94
Tonsils and adenoids (cases in which removal was advised)	102
Teeth (cases in which treatment was advised)	98
Frequent colds	125
Total	1,472

TABLE 4.—*Frequency of Defects*

Number of Defects	Number of Cases*
0	15
1	46
2	69
3	64
4	77
5	48
6	45
7	19
8	10
9	5
10	2
11	0
12	0
13	0

* Sixty-nine children presented two defects while only two children had ten.

TABLE 5.—*Causes for Failure*

Cause	Number of Cases
Poor cooperation	184
Failure of parents to improve	64
Unchanged environment	35
Physical conditions untreated	27
Transferred to private physicians	20
Moved before much was done	18
Inability to return	4
Wrong methods advised	1
Nonremedial	1
Total	354

Table 5 gives the causes for the failures. The numbers here given refer not to the number of children examined but to the number of defects that could not be remedied; that is, in a child listed as having four defects if two were remedied and two were not, two failures were recorded. The two most important causes of failure were poor

cooperation on the part of the parents and failure of parents to improve even though they tried to cooperate. Some of these failures could have been obviated by previous proper training of parents, but in others the cause of failure lay in temperamental defects which no amount of training could change.

To conclude, it has been wisely said that before the age of 6 years the character and emotional patterns of the child have been formed for life. If this is true, then the best time for a program of mental hygiene is during the preschool years, and the preschool clinics should consider the emotional side of the child's life as of equal if not of more importance than the physical side.

PATHOGENESIS OF ACUTE SEROFIBRINOUS PLEURISY*

ARVID WALLGREN, M.D.
GOTHENBURG, SWEDEN

Acute serofibrinous pleurisy is now almost invariably regarded as due to tuberculosis. In what manner tuberculosis gives rise to it, is, on the other hand, somewhat obscure. As a rule, one has been content to state that the tuberculous infection in some manner produces the exudation. The most obvious and common explanation is that a subpleural tuberculous focus has provoked an irritation of the pleura.

That a local tuberculous focus in the lung or the bronchial glands constitutes an important factor in the genesis of pleurisy is indicated by the fact that a focus of this kind can be detected on the side on which the exudation subsequently arises. If an opportunity presents itself of examining a child a short time before it contracts pleurisy, there are generally found homolateral hilar changes or a homolateral primary focus. Of fifty children examined before the development of pleurisy, forty-eight showed homolateral changes of this kind; in one of the fifty cases, no definite changes were observed, and in one the changes that were established by roentgen examination were on the opposite side. In the few cases, too, in which anatomic control could be effected, subpleural tuberculous foci were found on the same side.

One may assume from this that in those in whom acute pleurisy develops there is direct aggression of a tuberculous focus on the pleura. Clinical experience with this form of pleurisy, however, reveals several facts which make it probable that the assumption of a local irritation of the pleura does not constitute an exhaustive explanation of its origin. I will here deal with some of these facts.

Local pleural irritation caused by a subpleural glandular or pulmonary tuberculous focus does not lead to acute serofibrinous pleurisy in all circumstances. In pulmonary tuberculosis, it is, as one knows, not unusual to find, clinically, a local irritation of the pleura, but the result is generally a dry, localized pleurisy. In postmortem examinations of tuberculous corpses, one often finds anatomic tuberculous changes in the pleurae, but an accumulation of fluid is often lacking, despite the fact that the serous membranes may be free.

* Submitted for publication, July 10, 1929.
* From the Medical Department of the Children's Hospital.

Besides the local pleural irritation, something else is evidently required for this irritation to become an acute serous inflammation: The pleura must have the particular predisposition that this reaction seems to postulate.

Certain circumstances indicate that a certain constitutional factor is of importance for the appearance of acute pleurisy. Racial, as well as family, predisposition can be established.

While it may be assumed that, roughly speaking, the tuberculous illnesses, namely, glandular tuberculosis, bone and joint tuberculosis and pulmonary tuberculosis, are prevalent among children equally in different countries, it is striking how the occurrence of pleurisy varies in different countries. It is common in Scandinavia and comparatively rare in Central and Southern Europe and in the United States. I shall just mention in illustration that at the pediatric clinic in Breslau, Germany, there have been observed only twenty-six cases of pleurisy in twelve years,[1] while at the children's hospital in Gothenburg from thirty to forty pleuritic children are received every year. There is, of course, no reason to believe that the subpleural site of primary tuberculosis is commoner in Scandinavia than elsewhere. This condition for the appearance of pleurisy may be regarded as fairly uniformly present in different countries; but what is different is the way in which the person who has an irritation of the pleura from a subpleural focus reacts.

The common phenomenon of brothers and sisters, or of one of the parents and the children, contracting pleurisy points to a certain predisposition in the family. More especially, those who have been previously attacked by erythema nodosum have a predisposition to pleurisy. Of 290 patients with acute pleurisy, seventy-four had had erythema nodosum, and of all those who had had erythema nodosum 26 per cent were afterward taken ill with pleurisy. Just as several children in one family may get erythema nodosum at the same time,[2] so most of the children in one family may get pleurisy at about the same time.[3] Such endemics of pleurisy among brothers and sisters have been observed by me several times.

A certain predisposition is also attributable to the age, if one may judge from the great rarity of serofibrinous pleurisy in infants and very old people.

All these facts seem to me to prove definitely that whether the local pleural irritation is to become an acute serous pleurisy or not depends

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1. Knauer: Ztschr. f. Tuberk. **50**:403, 1928.

2. Wallgren: Beitr. z. Klin. d. Tuberk. **53**:143, 1922; Acta pædiat. **5**:225, 1926.

3. Wallgren: Paratuberkulöse Krankheitserscheinungen, in Engel-Pirquet: Handbuch der Kindertuberkulose, Leipzig, 1929.

in many respects on the way the person reacts. I shall try to analyze this constitutional character.

It is doubtless common knowledge that acute serofibrinous pleurisy is an exceptional complication of an already existing pulmonary tuberculosis, whereas it is by no means a rare precursor of this illness. Pleurisy has evidently a certain period of predilection, which comes before phthisis sets in. On the other hand, pleurisy, viewed purely anatomically, does not constitute the first manifestation of tuberculosis. I have never seen pleurisy set in at the end of the tuberculous incubation, just when allergy commences. This manifestation of the illness is common, however, immediately following the commencement of allergy. The time for the beginning of the pleurisy in relation to the commencement of allergy can be given fairly exactly for those who have suffered from erythema nodosum. By investigations, especially those of Swedish physicians,[4] it has been proved that the erythema nodosum that appears as the first manifestation of tuberculosis, breaks out just as the allergy commences, and is thus an outward sign that

TABLE 1.—*Intervals Between the Occurrence of Erythema Nodosum and the Occurrence of Pleurisy*

Interval, months	1	2	3	4	5	6	7	8	9	more than 9
Cases	4	8	11	11	10	10	3	0	1	16

the primary stage of tuberculosis has begun. If one knows, therefore, when a pleuritic patient has erythema nodosum, one can determine how long after the manifestation of the primary stage the pleurisy commenced. The interval between the erythema nodosum and the pleurisy in seventy-four cases is shown in table 1.

The table makes evident that in the majority of cases pleurisy appears within the first six months, with a maximum number of cases occurring within from three to six months, after the onset of allergy.

At this time, the allergy is strong, the reactionary power of the body is intensive, and the primary tuberculosis in lung and hilar glands is at its height. The whole organism is in a stage of supersensitiveness, including the pleura, and this makes it possible for an irritation from a subserous focus acting on a thus supersensitive pleura to lead to the rather violent reaction that acute serofibrinous pleurisy represents.

A characteristic feature of this form of pleurisy is its acute beginning. While the person involved is, as it would seem, in the best state of health, he suddenly falls ill, with high fever and a rapid

4. Belfrage: Acta pædiat. **4**:183, 1925. Lundius: Acta tuberc. Scandinav. **4**:256, 1929. Wallgren: Acta med. Scandinav. (supp.) **16**:363, 1926; Acta pæd. **5**:225, 1926; Ztschr. f. Kinderh. **43**:543, 1927; Jahrb. f. Kinderh. **117**:313, 1927; Initial Fever in Tuberculosis, Am. J. Dis. Children **36**:703 (Oct.) 1928.

accumulation of pleural fluid. The temperature curves may be seen here. Another characteristic feature is the fairly uniform duration of the fever. As appears from table 2, the fever is fairly uniformly of three weeks' duration. If it is a case of an ordinary form of tuberculosis in the lungs, glands or pleurae, the intensity and duration of the fever, as well as of the general symptoms, vary considerably, depending on the activity, diffusion, etc., of the pathologic process. With acute serous pleurisy in children, however, it is a question of a symptom-complex, which in different cases is fairly similar, with a typical commencement and course. This indicates that in pleurisy something different from the local tuberculosis, as such, determines the origin and course of the fever.

TABLE 2.—*Duration of Fever in Acute Serofibrinous Pleurisy*

Duration, weeks	1	2	3	4	5	6	7	8	9
Cases	1	23	79	17	6	5	4	1	1

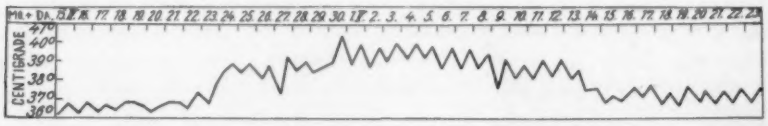

Chart 1.—Temperature curve in a case of acute serofibrinous pleurisy.

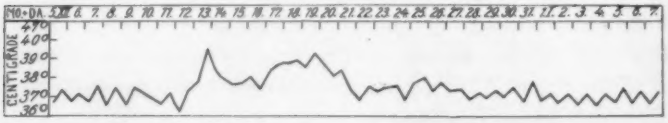

Chart 2.—Temperature curve in a case of acute serofibrinous pleurisy.

These clinical facts, therefore, point to the conclusion that it is only when the irritation from the intrathoracic tuberculous focus strikes a pleura that is in a condition of supersensitiveness caused by the tuberculous infection that the irritation gives rise to acute serofibrinous pleurisy. The ease with which such a condition of supersensitiveness arises, and its intensity, differ in different persons, and it is presumably in this manifestation that the constitutional predisposition of certain persons to pleurisy may be sought.

Certain experimental investigations in animals seem to support these clinical observations and deductions. Reports of conforming experiences have been gathered from different countries[5] showing

5. Arloing and Thevenet: Rev. Tuberc. **4**:553, 1923. Corper and Rensch: Am. Rev. Tuberc. **4**:763, 1920. Patterson: ibid. **16**:29, 1927. Péron: Dissertation, Paris, 1896.

that if healthy animals are inoculated intrapleurally with tubercle bacilli, pleural tuberculosis is certain to develop, but that no disease occurs which resembles acute pleurisy in man. If, on the other hand, the intrapleural inoculation is made into animals that have been tuberculous for several weeks, there develops, according to Paterson,[5] acute pleurisy. The pleura is thus held to react in a different way in an already tuberculous animal from the way it reacts in a healthy one, and the pleurisy in this case is interpreted as an immunity reaction.

The experience thus gained from experiments on animals has been applied to man, and the manner in which pleurisy develops is thus described by Bezançon and Philibert:[6] When acid-fast bacilli attack the apparently normal pleura in a previously infected organism, in which the pleura, as well as the whole organism, has been sensitized by the first infection, there occurs a strong reaction, with hyperemia and exudation of serofibrinous fluid. The ordinary reaction, with tubercle formation and caseation is, on the other hand, absent or obscured.

The reinfection of the pleura in pleurisy in man is of course to be regarded as endogenous, arising from a focus situated near the pleura. Probably, it is not necessary for the irritation to be caused by a living virus. A toxic irritation from the tuberculous focus can undoubtedly also give rise to acute pleurisy; as a rule, this is probably the case, if one may judge from the comparatively slight frequency (about 25 per cent) with which tubercle bacilli can be detected in the exudation of pleuritic children.

SUMMARY

The facts that have been discussed in this article seem to me to favor the view that the pathogenesis of acute serofibrinous pleurisy must be conceived of as follows: At a certain time after the tuberculous infection has taken place, the whole organism, including the pleurae, becomes hyperirritable. Through a subpleurally situated tuberculous focus in the lung or the hilar glands, a local irritation is set up in the pleura. This irritation can, as a rule, be caused by toxins generated in the tuberculous focus, but sometimes there is also a bacillary invasion with formation of tubercles. The effect of this endogenous reinfection or toxic irritation of the hypersensitive pleura is a violent reaction with fever and a rapid accumulation of serofibrinous fluid in the pleural sack. The whole phenomenon is to be regarded as one of hypersensitivity, and pleurisy, therefore, as an allergic manifestation of tuberculosis.

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6. Bezançon and Philibert: Paris méd. **1**:11, 1926. Bezançon and Weil: Monde méd. Paris, 1926, vol. 65; Ann. de méd. **21**:266, 309, 331 and 344, 1927.

Pediatric Biographies

WOLFGANG HOEFER
1614-1681

JOHN RUHRÄH, M.D.
BALTIMORE

Little is known about Wolfgang Hoefer, but he is given a page in pediatric history on account of his description of cretinism, probably the first extended account of that condition. His father was a professor of medicine. Wolfgang was born in Freising in upper Bavaria. He studied medicine at Ingolstadt, and, after traveling in Italy and France, settled there. Like many of the physicians of his time he practiced in various places, in Straubing, in Linz, at Raab in Hungary, and finally in Vienna, where he was made K. K. Hofrath. His one book, entitled "Hercules medicus, sive locorum communium, tomus unicus," was published in Vienna in 1657, and reprinted there in 1664 and also at Nuremberg in 1665 and 1675.

The cretin, when he has a goiter, as in those described by Hoefer, reminds one, as Osler once remarked, of the description in Shakespeare's "Tempest."

> "Mountaineers
> Dew-lapp'd like bulls, whose throats had
> hanging at 'em
> Wallets of flesh."

Another classic reference frequently mentioned is to be found in the thirteenth satire of Juvenal, line 162-163.

> "Quis tumidum guttur miratur in alpibus, aut quis
> in Meroe crasso maiorem infante mamillam."
> Who marvels at a swollen throat in the Alps?
> Or who in Meroe at a woman's breast bigger than her sturdy babe?

Hoefer, like most physicians of his time and many of today, was fond of discussing things about which he was not correctly informed instead of confining himself to the facts. Part of his description is as follows:

FOOLISHNESS

Because foolishness (*stultitia*) is so familiar in very many inhabitants of the Alps, and indeed is endemic, some ascribe it to the *air*, others to *water*, still others to *food* and *education*.

But beware lest you decide upon the *first*. Otherwise you may be exposed to the same reply as the man, who, when he was falsely censuring the foolishness

of these men and was sharply arraigning the defect of the *air,* while he was using this locality in a liberal manner and enjoying the same air as guest, heard the following reply: "Depart quickly, good sir, lest, infected by the same air, even you yourself must needs be foolish in company with us."

Not the *second,* because to many inhabitants of the Alps *waters* are very healthful to drink, and yet very many of them are foolish.

Title page of Wolfgang Hoefer's "Hercules Medicus."

Therefore the *third* will hold: *food* and *education.* And this opinion is borne out by other considerations in my frequent examination of their diet and mode of life. For this is a class of people, who delight in foods which supply much excrement, but little aliment; they are displeased with the opposites; on this account they are voracious, yet never full, except to the point of bursting when the abdomen bends. Their children, in this manner stuffed at least four times a

day, they deposit near the oven, and instruct them neither in letters nor in morals nor in labors, frequently they pay no attention to their (children's) entreaties, so that, when their food also aids their melancholy and gloomy spirits, they are necessarily made *stupid* and *foolish*.

They also become *strumous* from almost the same cause. For while the children are thus neglected and leisurely subside into themselves "they pile upon one another by the oven" like dogs, devouring choice bits with full jaws; they distend and dilate the skin and the little glands around the neck; and because their heads are filled with gloomy vapors by similar food, the latter, being turned into liquid and flowing down, are drunk in by the glands or form new glands and monstrous strumas.

Now it must not be entirely denied that such *hernias* of the throat, called *bronchocele* or *strumas* by the Alpine inhabitants themselves, as if an endemic disease, can be contracted by a common potion of *water* tinged with mercury, which, by a singular characteristic which it possesses, causes rheumatisms, fatigues the jaws and teeth and joins tumors, as Reusner, "Tractatus de scorbuto," rightly gives as his opinion. Now the inhabitants themselves, when questioned, advise travelers to abstain from these springs, having learned from experience that walking-sticks immersed and withdrawn shortly afterward have become deformed by very many knots and uneven. But because such springs are very rare, I have decided to agree to the opinion adduced and demonstrated above; with this one addition, that through such a mode of life the power of reproduction is not lost, and therefore also by an *hereditary* evil the parents communicate *foolishness* to their offspring.

I said above that these Alpine dwellers are displeased by better and more refined food. For example, take at least the sole one, which, though most distasteful to others, they nevertheless consider among their delicacies and call, in their own idiom, *muncken*. Oats, just as they are, crushed with a millstone, they cook in a baking-pan, with water, sprinkled with a dash of salt, until it takes on the form of peeled barley. Then, when a large enough opening has been made in the middle, they pour in melted lard, zerlassen Schmalz, and dipping a spoon therein they separate a part of the fast-clinging porridge and devour it.

News and Comment

CLINICS

The Children's Fund of Michigan announced, on August 27, that a series of clinics for children will be maintained in Menominee County from three to five years at the annual expense of from $25,000 to $30,000.

GENERAL

The Second International Pediatric Congress in Stockholm.—After having conferred with and received the promise of support from leading pediatricians in practically all the countries of the world, the Swedish pediatricians issue invitations to an international pediatric congress in Stockholm, Sweden, from Aug. 17 to 20, 1930.

Notification of lectures is to be made before March 1, 1930, at the latest.

The program of the conference will, if necessary, be carried on in separate groups.

It is desirable that those wishing to attend signify their intention of doing so as soon as possible, so that the approximate number to be expected may be calculated, and arrangements made in good time for their housing and comfort. This is of great importance because of the Swedish Art and Industry Exposition which will be going on in Stockholm during the summer of 1930.

The admission fee to the conference is 20 Swedish crowns.

All communications are to be addressed to The Second International Pediatric Congress, Stockholm, Sweden. The telegraphic address is Pediatric, Stockholm.

Applications for tickets of admission should preferably be accompanied by the fee, sent as a check or a money order.

For the avoidance of errors, it is absolutely necessary to print or typewrite names and addresses.

Further announcements will appear later.

Members of the committee are: I. Jundell, M.D., professor of pediatrics, chairman; K. O. A. Klercher, M.D., professor of pediatrics, Lund; R. Nordgren, M.D., chairman of the pediatric section, Swedish Medical Association, Stockholm; I. Thorling, M.D., professor of pediatrics, Upsala; W. Wernstedt, M.D., professor of pediatrics, Stockholm, and Nils Malmberg, M.D., lecturer in pediatrics, Stockholm, secretary.

Infant Paralysis Clinic in Tennessee.—The state health department of Tennessee opened its first infantile paralysis clinic at Knoxville, Tenn., August 24. Fifty-three cases of infantile paralysis were reported in the state. A survey of the extent of malarial disease among school children has been undertaken in Tipton County, Tenn. Specimens of blood from about 2,000 children were sent to a central laboratory to be examined for malarial parasites.

Bequests and Donations.—The St. Louis Children's Hospital, St. Louis, was given $40,000 by the will of Walter C. Taylor.

The Home for Destitute and Crippled Children, Chicago, was willed the entire estate of Frederic R. Skillman, D.D.S., Oak Park, Ill., which amounted to about $350,000. The greater part of the income will go to the widow, and after her death, to the home.

The Country Home for Convalescent Children, University of Chicago, received $60,000 from Mrs. James N. Raymond to erect a building on the Du Page site of the home.

UNIVERSITY NEWS

Dr. Jose Zamarriego, associate professor of the faculty of medicine at Madrid, Spain, has been called to the chair of pediatrics at Cadiz.

Correspondence

COMMENTS ON THE ARTICLE, "CERVICOVAGINITIS," BY DR. STEIN ET AL.

To the Editor:—An article in your June issue by Drs. Stein, Leventhal and Sered, entitled "Cervicovaginitis," I feel is of considerable interest and importance. As these authors noted, Hess' observations on autopsy material long ago called attention to the presence of "cervicitis" as a factor in the stubbornness of infections of the lower genital tract in female infants and children. I also called attention to clinical observations of the same condition in October, 1927. An important point that was not stressed in Dr. Stein's recent communication is that this "cervicitis" is in the vast majority of cases strictly a cervicitis and not an endocervicitis. This point was made clear by Hess and has been verified in my experience, almost without exception. The condition, then, since it involves the vaginal portion of the cervix and seldom the endocervix, is really an integral part of the vaginitis. That this is true is definitely indicated by the reaction to ointment applied simply to the vagina. I am sure that Dr. Stein agrees with me on this point, but he has not made it clear in his recent article. I have called attention to this because of the inadvisability under ordinary circumstances of attempts to treat the infantile endocervix. Attempts to accomplish this by topical applications in these small patients are certainly less effective than similar attempts in adults, and their ineffectiveness in adults is realized only too keenly.

Possibly due to an error of the printer, Dr. Stein's suggestion in regard to the use of "hydrous wool fat" appears incorrect. No doubt he means anhydrous wool fat, as suggested in this connection by myself two years ago. Hydrous wool fat, by actual test, is about 30 per cent less absorptive and does not possess the body and tenacity which characterize the anhydrous substance. I am unable to appreciate the need for the dilution of this ointment base with petrolatum. I should think the quality of tenacity to moist tissue would be destroyed by the introduction of an ordinary grease constituent which is repulsed by moisture. Also, would it not seem rational to create at least a mild amount of intravaginal pressure in order to distend the crypts and rugae which characterize the immature vaginas, thereby achieving a complete application?

One further suggestion is offered. The use of such an instrument as has been devised by these authors is of unquestionable value. However, as Dr. Martzloff and I have found, a small female urethroscope with a head mirror (not a seed lamp), as also formerly suggested, is satisfactory, provided the special instrument is unobtainable.

GOODRICH C. SCHAUFFLER, M.D., Portland, Ore.

DR. IRVING F. STEIN'S REPLY TO THE COMMENT OF DR. SCHAUFFLER

To the Editor:—In reply to the recent communication of Dr. Schauffler, I wish to thank the doctor for his interest and his kindly criticism. In regard to the ointment, I have used hydrous wool fat, mixed with petrolatum and 1 per cent mercurochrome-220, ever since we first began our work on vulvovaginitis in 1921. Hydrous wool fat, according to Cushney (edition 4, p. 50), "is miscible in twice its weight of water without losing its ointment consistency," and therefore is capable of absorbing the vaginal moisture completely.

I have not materially changed our technic of treatment in the past seven years except for the additional use of the vaginoscope in the study of our patients. Will you kindly refer Dr. Schauffler to our former publications (A Clinical Investigation of Vulvovaginitis, Surg. Gynec. Obst. **36**:43 [Jan.] 1923; A Bacteriologic Study of Vulvovaginitis in Children, J. Infect. Dis., **32**:444 [June] 1923; The Mercurochrome Ointment Treatment of Vulvovaginitis, Illinois M. J. **45**:219 [March] 1924), as well as to the chapter on this subject in Abt's Pediatrics, vol. 6, published in 1925, all of which predated Dr. Schauffler's article? He has apparently used a modification of our method with success. As our most recent contribution (Cervicovaginitis, Am. J. Dis. Child. **37**:1203 [June] 1929) was a further report of our original work, no attempt was made to include a complete bibliography.

IRVING F. STEIN, M.D., Chicago.

Miscellany

REPRODUCTION OF PHOTOMICROGRAPHS

The reproduction of photomicrographs in this journal is limited by the available space on the page.

The column width is 4¼ inches. All cuts have a ⅛ inch shoulder on each side to permit of the metal being fastened to the wood block; hence, if consistent with the material to be shown, illustrations are reduced to column width—that is, to 4 inches. Larger cuts not only cost more but necessitate additional expense in arranging makeup. When necessary or especially desirable, larger reproductions can be produced, but only in very exceptional instances are cuts made more than 5½ inches wide.

When photomicrographs more than 5½ inches wide are submitted, authors should decide whether they prefer to have only the significant portion of the illustration reproduced full size or to have the entire picture shown with reduction. Notation of the choice should accompany the manuscript; in case choice is not indicated, manuscript editors will use their own judgment as to the procedure to be followed.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE BLOOD SEDIMENTATION TEST IN EXPERIMENTAL POLIOMYELITIS. J. R. KAGAN, Am. J. M. Sc. **78**:67 (July) 1929.

The author discusses the sedimentation test in various diseases and also outlines the Linzenmeirer technic which was used in his series of cases. His experimentations were made on monkeys.

Table 1 gives readings of a group of normal monkeys showing the average sedimentation time of nineteen hours and thirty-two minutes. Table II shows the sedimentation reactions in a group of monkeys having tuberculosis; the average sedimentation time was one hour and twenty minutes. Table III gives the sedimentation time in cases of experimental poliomyelitis in twenty monkeys, showing the average sedimentation time of two hours and thirty-nine minutes. Table IV shows the readings in miscellaneous cases. Those of general debility showed an average time of sedimentation of thirty-five minutes; four infected skins showed an average time of sixty minutes.

Kagan's experiments on sedimentation time show that the period of the normal healthy monkey is nineteen hours and thirty-two minutes. In monkeys sick with poliomyelitis, the average sedimentation time is two hours and thirty-nine minutes. In monkeys sick with tuberculosis or general debility of undetermined nature with superficial infection, the time is still shorter.

HENSKE, Omaha.

DIABETES INSIPIDUS — THE DIURETIC SUBSTANCE. H. BOURQUIN, Am. J. Physiol. **88**:519, 1929.

A diuretic substance has been found in the urine of dogs with experimental diabetes insipidus, which is not found in the urine of normal dogs. Such a substance has been demonstrated in extracts of large amounts of the mamillary bodies and thalamus of the brains of normal animals, and is not found in any appreciable quantity in other parts of the brain. Both diuretic substances are destroyed by strong alkaline solutions at room temperature, are destroyed by ashing, are not dissolved by ether, acetone or 95 per cent alcohol, are precipitated by barium hydroxide from somewhat alkaline solution, and are not precipitated by phosphotungstic acid. From their similarities in these respects, it may be inferred that they are identical.

H. E. EGGERS.

THE TESTICULAR ALLERGIC RESPONSE IN GUINEA-PIGS FOR THE DIAGNOSIS OF TUBERCULOUS FLUIDS. J. J. WIENER, JOHN E. BLAIR and HENRY L. JAFFE, Am. Rev. Tuberc. **19**:55, 1929.

In making a diagnosis, an attempt was made to apply Long's testicular tuberculin reaction to the body fluids suspected of coming from tuberculous foci. The test consists of the injection of from 0.1 to 0.3 cc. of the suspected fluid into the testis of a tuberculous guinea-pig, autopsy on the animal after from five to seven days, and the histologic examination of the testis for a characteristic degeneration. The diagnostic value of the test is impaired by the fact that about 35 per cent of nontuberculous fluids (particularly fluids from patients with malignant tumor) gave a reaction which was histologically indistinguishable from that given by tuberculous fluid. Data obtained show that this is a toxic effect, which apparently cannot be eliminated by reduction of the amount of fluid injected. However, if from 0.1 to 0.2 cc. of the fluid from a suspected tuberculous focus, with the exception of spinal fluids, does not produce the aforementioned reaction, on inoculation into the testis of a tuberculous guinea-pig, the possibility of tuberculosis of that focus may be definitely ruled out.

H. J. CORPER.

EXPERIMENTAL DIABETES INSIPIDUS. E. B. TOWNE, Arch. Surg. **18**:1165 (April) 1929.

Towne attempted to produce diabetes insipidus in dogs by detaching the stalk of the pituitary gland. He found that the polyuria thus produced was transitory. He has searched through the literature and found that separation of the stalk rarely if ever produced permanent polyuria. From his experiments and from the literature, he feels that the neurogenic theory of Camus and Roussy is not supported. He believes that these experiments strongly suggest that diabetes insipidus is due to suppression of the secretion of the pars intermedia and the pars tuberalis.

GRANT, Philadelphia.

SURVIVAL OF THE VIRUS OF POLIOMYELITIS FOR EIGHT YEARS IN GLYCEROL. C. P. RHOADS, J. Exper. Med. **49**:701, 1929.

An instance of successful inoculation of poliomyelitis virus after preservation for eight years in 50 per cent glycerin is reported. The virulence of the material injected remained essentially unchanged during this period. The fact that poliomyelitis virus will survive in glycerin for so great a period may be taken as further indication of the improbability of streptococci as the inciting organisms. Poliomyelitis virus would seem to vary in its resistance to glycerination. The remarkable persistence of active virus outside of the body may have a bearing on the epidemiology of poliomyelitis.

AUTHOR'S SUMMARY.

HYPERSENSITIVENESS TO DIPHTHERIA BACILLI. JAMES M. NEILL, WILLIAM L. FLEMING and EMIDIO L. GASPARI, J. Infect. Dis. **44**:150, 1929.

In this study of the skin reactions to injections of diluted diphtheria culture filtrate, a group of 1,350 adults was tested with injections of 8×10^{-4} cc. of heated (80 C.) filtrate, and of the same amount of broth culture medium. Immediate reactions that could be referred to the diphtheria bacterial derivatives occurred in only four persons, 0.3 per cent of the group. Reactions to injection of the test dose of diluted broth, on the other hand, were common, significant ones being observed in 18 per cent of the group. Most of the responses to the injection of diluted broth could be referred to actual constituents of broth, but some reactions were apparently due to trauma alone. A general outline is given by which the skin reactions to intradermal injections of the whole bacterial filtrate may be distinguished.

AUTHORS' SUMMARY.

PASSIVE TRANSFER OF HYPERSENSITIVENESS TO DIPHTHERIA BACILLI. JAMES M. NEILL and WILLIAM L. FLEMING, J. Infect. Dis. **44**:224, 1929.

The three types of skin reaction to diphtheria bacterial derivatives are differentiated in this paper by passive transfer experiments. The capacity for the immediate hypersensitive reaction to heated diphtheria filtrate was transferred to from 61 to 103 persons by the Prausnitz-Küstner technic; the capacity for the delayed or pseudo reaction to the same heated filtrate failed of transference. Serum from persons without the pseudo reaction had no neutralizing effect when previously injected into the skin of persons with pseudo reactivity; serum from a person with a negative Schick reaction transferred local antitoxic immunity to skin areas of persons with positive Schick reactions, as indicated by neutralization of toxin injected two days after introduction of the serum.

The success or failure of the Prausnitz-Küstner technic to transfer to local skin areas the types of antidiphtheria immunity represented by the three different skin reactions is illustrated. The results showed that active antidiphtheria immunity had no relation to a person's response in the passive transfer of the immediate skin reaction to the culture filtrate of the same bacteria.

AUTHORS' SUMMARY.

HYPERSENSITIVENESS TO DIPHTHERIA BACILLI AND RAGWEED POLLEN. WILLIAM L. FLEMING and JAMES M. NEILL, J. Infect. Dis. **44**:308, 1929.

The investigation consisted of a quantitative correlation of the responses of a group of people to ragweed pollen extract, in skin locally sensitized by ragweed hypersensitive serum, with the responses of the same persons to diphtheria culture filtrate in skin locally sensitized by diphtheria hypersensitive serum. Proper quantitative relationships between serum and test substance were established by preliminary experiments. The final tests for comparison were made on sixty-four persons. When the pollen-antipollen and bacterial-antibacterial systems were properly adjusted, the skin response of each person to one antigen was approximately the same as his response to the other; in most cases, they were identical. The quantitative correspondence in the individual transfer responses to the bacterial and nonbacterial antigen are illustrated. The results were discussed both from the standpoint of their significance in the study of diphtheria bacterial hypersensitiveness and from the standpoint of their theoretical interest in the study of hypersensitiveness in general.

AUTHORS' SUMMARY.

THE BLOOD SUPPLY OF THE THYROID GLAND WITH SPECIAL REFERENCE TO THE VASCULAR SYSTEM OF THE CRETIN GOITRE. O. H. WANGENSTEIN, Surg. Gynec Obst. **48**:613, 1929.

The blood supply of thirty-nine thyroid glands was studied after intra-arterial injection, with the glands submerged in physiologic solution of sodium chloride, some following the instillation of diluted ink; in a few cases, roentgen examinations followed the injection of mercuric oxide and Hill's white paste. The inferior thyroid artery was found to be considerably larger than the superior, and in several of the cretin goiters the former had a diameter of 9 mm. In the seventeen specimens from necropsy the inferior thyroid was absent but the superior was always found; in two the vessel was small. One gland had a double superior thyroid artery. An accessory thyroid artery was observed twice in dissected postmortem specimens. An anomalous artery, in one cretin patient, which arose as a branch from the main division of the right superior thyroid artery ran obliquely across the isthmus and communicated with the left inferior thyroid artery. The free anastomosis between the subcapsular vessels was well demonstrated in the various methods of injection. There seemed to be no direct relation between the size of the goiter and its arteries. A few injections of the veins revealed great friability of their walls with rupture and dissemination of the injected material into the adjacent tissue.

In cretin goiters intimal thickening was frequently observed, and in many instances almost complete occlusion of the lumen was noted in the arteries of the capsule and in those of the second order; even the follicular and interlobar branches were the site of degenerative changes. The muscular walls of the larger groups of vessels were often very thin. The interfollicular network of colloid goiters was narrowed and compressed, and their capillary communications were often absent. The adenomatous glands revealed changes similar to those of the cretin goiters; in both, areas of hyperplasia were surrounded by capillaries which appeared more like the normal vessels. This marked enlargement of the extraglandular vessels is regarded as a compensatory effort to bring as good blood supply as possible to the adenomatous areas of physiologically hypo-active tissue, as alterations in the stroma have made a normal nutrition impossible.

RICHARD A. LIPVENDAHL.

ANTI-VACCINAL SERUM. C. H. ANDREWES, J. Path. & Bact. **32**:265, 1929.

Generalized lesions appeared on the skin of 79 per cent of rabbits inoculated intradermally with a testicular strain of neurovaccine. This generalization could be prevented by giving comparatively small doses (3 cc.) of immune serum intravenously. Generalized lesions always appeared on the skin of rabbits inoculated intravenously with more than 500 skin-infecting doses of neurovaccine. Here, also,

generalization could be prevented by giving intravenous serum before or mixed with the virus. With the serums used, approximately 1 cc. was necessary for every 1,000 minimal skin infecting doses of virus. Fifty-five per cent of the rabbits in which the serum prevented generalization were found on subsequent test to have developed an active immunity. Serum which reaches the tissues five minutes before the virus is far more effective than when the virus is five minutes ahead of the serum. This is most easily shown by "local passive immunity" experiments in the rabbit's skin.

AUTHOR'S SUMMARY.

INVOLUTION AND REGENERATION OF THE THYMUS UNDER THE INFLUENCE OF BENZENE. J. E. LEWIN, Virchows Arch. f. path. Anat. **268**:1, 1928.

The ingestion of benzene leads to atrophy of the thymus in the rabbit, the picture of "accidental involution." There are two stages: the formation of an inverted gland and the period of connective tissue development with atrophy of lobules. The first period is characterized by a rapid lymphocytic disintegration and activity of the reticulo-endothelial cells. The latter cells hypertrophy, become isolated and form free macrophages, hemocytoblasts which in turn develop into pseudo-eosinophils, premyelocytes and myelocytes. In the second period besides an overgrowth of interlobular connective tissue, there is formed a close meshed network of collagen bundles within the lobules. The reticular cells play a prominent rôle in the formation of new lymphocytes, a lesser rôle by the adventitial cells. The regeneration of the thymus is accompanied temporarily by myelopoiesis and erythropoiesis, most pronounced in the cortex.

V. C. JACOBSEN.

THE INFLUENCE OF CHOLESTEROL ON EXPERIMENTAL ANAPHYLAXIS. L. SURANYI and L. JARNO, Ztschr. f. Immunitätsforsch. u. exper. Therap. **56**:303, 1928.

Reinjection with cholesterinized serum does not prevent anaphylaxis. Animals in which the blood cholesterol is increased by cholesterol feeding before reinjection succumb without exception to anaphylactic shock. Blood with an increased cholesterol content contains a decreased amount of complement. An interrelation exists between the decrease of complement in anaphylaxis and in cholesteremia and the anaphylactic disposition in cholesteremia.

W. C. HUEPER.

Nutrition

TISSUE CHANGES ASSOCIATED WITH VITAMIN "A" DEFICIENCY IN THE RAT. M. DAWSON TYSON and ARTHUR H. SMITH, Am. J. Path. **5**:57, 1929.

The principal changes associated with vitamin A deficiency in rats are a metaplasia of cuboidal or columnar epithelium in certain parts of the body, epithelial hyperplasia in various structures and infection. The metaplastic changes involve the following structures in order: the sublingual glands, the submaxillary glands, the epithelium of the renal pelvis and of the trachea and bronchi. The tongue is regularly involved before xerophthalmia appears. The serous type of sublingual gland is the first to be affected. The lesion in the tongue and submaxillary gland begins with a dilation of the ducts and a metaplasia of the lining epithelium accompanied by infection. In late cases the glandular tissue may be entirely destroyed by pressure from the dilated ducts and by necrosis due to infection. The submaxillary gland is not involved as constantly as the tongue. The epithelium of the renal pelvis may be involved fairly early. Metaplasia and infection are always present in the advanced cases. Renal calculi are prone to occur and when obstruction to the urinary outflow is present, pyonephrosis develops which is sometimes followed by perinephric abscess. Epithelial metaplasia of the trachea and bronchi is not common. The most usual observation is an atrophy of the lining cells. Epithelial hyperplasia is striking in the tongue and renal pelvis. In the latter the hyperplasia overshadows the keratinizing process.

Infection is always present even in the earliest stages and in late cases dominates the picture. No metaplastic activity has been seen without an accompanying infection, but infection has been observed in parts where metaplasia is absent. If the results of the dietary deficiency are not too severe, xerophthalmia clears rapidly with the administration of cod liver oil, and the weight curve rises abruptly. The extent of healing in the various organs depends largely on the amount of destruction due to infection which is present. Following the administration of cod liver oil, abnormal epithelium and chronic or acute infection persist in the tongue and renal pelvis when the rat is apparently healthy.

AUTHORS' SUMMARY.

THE PROTEINS OF EGGWHITE. LUDVIG HEKTOEN and ARTHUR G. COLE, J. Infect. Dis. **44**:165, 1929.

Tests made with the precipitin reaction indicate that crystallized ovalbumin, when subjected to putrefactive processes, is not converted into conalbumin. It has also been shown that such a putrefying solution of ovalbumin loses its power to react with its specific antiserum even while it still contains a considerable amount of coagulable protein.

AUTHORS' SUMMARY.

THE NERVOUS SYSTEM IN RATS FED ON DIETS DEFICIENT IN VITAMINS B_1 AND B_2. RUBY O. STERN and G. MARSHALL FINDLAY, J. Path. & Bact. **32**:63, 1929.

Rats fed on a diet deficient in both vitamin B_1 and B_2 exhibit only slight chromatolytic changes in the ganglion cells of the cord. Rats fed on a diet deficient in vitamin B_1 exhibit the same changes but to a greater extent for the same duration of life. In addition, when symptoms of paralysis are of long standing, early degeneration may be found in the myelin of the peripheral nerves. The histologic changes found in the nervous system of rats fed on a diet lacking vitamin B_2 consist in swelling and vacuolation of the anterior horn cells of the spinal cord with the deposition in them of lipochrome pigment, a noticeable increase in the surrounding satellite cells and an increase in the number of granules in the peripheral nerves.

AUTHORS' SUMMARY.

CHANGES IN THE THYROID GLAND IN AVITAMINOSIS B. S. A. SATWORNITZKAJA and W. S. SIMNITZKY, Virchows Arch. f. path. Anat. **266**:329, 1927.

In the thyroids of rats on a diet lacking in vitamin B, there was found at first increased secretory activity, with hypertrophy and new growth of follicles and increase in colloid. Later, rupture of several follicles occurred, with escape of colloid, along with necrobiosis of the follicle cells. Since no repair took place, this process was followed by decrease in the size of the gland. In the end-stage, signs of exhaustion and decreased function became evident, but not to any marked degree.

In the thyroids of pigeons the same changes were observed, except that evidence of terminal decrease in function was lacking. Necrobiotic changes in the single cells appeared to be the result of increased activity with disturbance in nutrition, in consequence of the vitamin lack. These changes were too slight, however, to account for a decrease in function.

The results present no evidence of significant decrease in secretion during vitamin B inadequacy, but, on the contrary, show an increase, for a certain length of time in rats, and until the end in pigeons.

B. R. LOVETT.

EXPERIMENTAL RICKETS. T. SKAAR and K. HAFUPL, Virchows Arch. f. path. Anat. **271**:100, 1929.

Young dogs were fed on Mellanby's rickets diet. After three weeks the first signs of rickets appeared. The dogs were sick, awkward in their movements, ate

little and did not gain in weight. Roentgenograms of the radius and tibia showed poor ossification, thickening of epiphyses, widening of epiphyseal lines and frayed surfaces of the joints. Addition of 40 cc. of cod liver oil daily effected a rapid cure; the bone thickenings disappeared but the curvatures persisted. The phosphorus and calcium metabolism of the rachitic dogs was negative. The phosphorus and calcium content was low. After cod liver oil was given, the serum phosphorus rose quicker than the serum calcium. The bone of the cured animal contained less phosphorus and calcium than that of the control animal (which had 10 cc. of cod liver oil daily). In some dogs the phosphorus metabolism was more damaged; in others, the calcium metabolism; there seem to be different forms of rickets. Large doses of phosphorus and calcium led to increase of phosphorus and calcium in the serum; but the bones of these dogs did not contain more phosphorus or calcium than those of the controls.

Nonlamellated bone was found in the controls also; it has nothing to do with rickets. Excessive formation of lime-free bone in the whole skeleton is characteristic of rickets. (N. Bock's method was used for demonstrating the lime-free bone). The lime-free layers were ten times thicker than in the controls. Periosteal deposits of bone were less marked than in human rickets, but much more intense than in the controls. They are not of primary importance in the diagnosis of experimental rickets. Osteoblasts and osteoclasts did not differ from those in the controls and no such differences exist in human rickets. There were no signs of halisteresis. The bone marrow of the rachitic dogs was fibrous; this is a secondary process due to irritation and stasis. The proliferating cartilage ("Knorpelwucherungszone") was from four to five times thicker than in the controls, occasionally from seven to ten times. The proliferating cartilage was vascularized from the marrow and from the perichondrium. The pathologic proliferations of the cartilage in the joint are secondary. It is the same with the formation of giant cells in hemorrhagic foci. The authors conclude that true rickets can be produced by deficient diet and cured by cod liver oil.

ALFRED PLAUT.

Prenatal Conditions

CONGENITAL VALVULAR OBSTRUCTION OF THE PROSTATIC URETHRA. H. H. YOUNG and R. W. MCKAY, Surg. Gynec. Obst. **48**:509, 1929.

The authors report fifty-one cases of congenital valvular obstruction of the urethra in persons from 11 days to 57 years of age. The condition is described as an obstructing fold of mucous membrane coming from the vesicle neck in the form of semilunar valves, as a diaphragmatic membrane below the verumontanum, or as a fold running downward from the prostatic orifice anteriorly. As a result of this obstruction to the outflow of urine, there is a funnel-shaped dilatation of the prostatic urethra and vesicle neck. If the obstruction is marked or if the condition is of long duration, the urinary bladder, ureteral orifices, ureters and the renal pelves may be markedly dilated. The authors divide the condition into three types depending on the position and character of the obstructing valves. The importance of early cystoscopic examination, the prognosis and the treatment are discussed.

RICHARD A. LIFVENDAHL.

CONGENITAL VALVES, PSEUDOVALVES AND STENOSIS OF THE PYLORUS AND DUODENUM. A. COSTA, Arch. di pat. e clin. med. **7**:501, 1928.

At the autopsy of a woman, aged 60, a valvelike formation was found in the pyloric canal; the basal attachment of this pyloric valve measured 2 cm. in width, 1 cm. in length and 3 mm. in thickness. In its close vicinity, there was another but smaller, tonguelike, mucous projection. Microscopically, it showed the structure of a normal mucosa (transition between pyloric and duodenal type) and contained a few smooth muscle cells, which were branching from the muscularis mucosae. The author classified this valvular formation of the pylorus, which was observed only once in about 20,000 autopsies, as a developmental dis-

turbance and as an excess in growth. The literature contains only one paper dealing with this subject, published by Arregger in 1896. These congenital valves of the pylorus should not be confused with pseudovalvular formations, which are the result of a benign neoplasm, as described by Magnus-Asleben, and which originate from a proliferation of glandular and muscular tissues (adenomyoma of the pylorus). The author then describes a typical case of a pseudovalve of the pylorus due to traction, microscopically an adenoma, in a man 67 years of age. Various forms of congenital pyloric stenosis are discussed in detail and, in accordance with Chiari, three types are introduced: (*a*) congenital stenosis of mucous type (stenosis of Landerer-Maier type); (*b*) congenital stenosis of muscular type (hypertrophic stenosis, stenosis of Hirschsprung type), and (*c*) congenital stenosis of combined type (a variety of Landerer-Maier type). The theories regarding the development of congenital stenosis of the duodenum and of the duodenal atresia are exhaustively presented. The studies of Schridde, Beneke and Tandler, which tend to prove an embryonal epithelial occlusion of the duodenum, are contrasted with the theories propagated by Marchand, Thorel and Fanconi, who assume the existence of a fetal enteritis.

E. L. MILOSLAVICH.

INFLAMMATIONS OF THE PLACENTA AND FETAL SEPSIS. FRIEDRICH WOHLWILL and HANS ERHARD BOCK, Arch. f. Gynäk. **135**:271, 1929.

Four cases of diffuse placentitis are described. The bacteria were *Bacillus coli* in two cases; streptococci in one case; and a mixed infection of gram-negative bacilli (*B. coli*) and gram-positive anaerobic bacilli in the fourth case. The pregnancies concerned were in the fourth and fifth month. The placentitis is regarded as secondary to fetal bacteremia. The organisms were distributed in large quantities in the placenta, especially the villous vessels which contained emboli of bacteria; other fetal organs as the liver, spleen and brain also contained large numbers of bacteria. The organisms in the villi had invaded the intervillous spaces through a break in the syncytial lining and thus infected the maternal blood stream. One mother died of sepsis which was considered secondary to the fetal septicemia, and another mother whose uterus was removed showed that the organisms had extended into the vessels of the broad ligaments. In the two other cases there were no or slight reactions in the maternal organism despite the diffuse distribution of bacteria in the fetus. One of these had an external thoracic defect which probably permitted direct entrance of organisms from the infected amniotic water. The case of streptococcal fetal infection was considered to be secondary to a maternal focus. In the other cases, the infection is thought to have been conveyed through the amniotic water, and the latter was thought to have been infected secondary to criminal interference with pregnancy. The reactions of the fetus and its ability to cope with infection are discussed. The placenta showed an accumulation of countless leukocytes about the villi, chorionic plate and about the amnion. There were regressive and progressive changes and phagocytosis. Despite the overwhelming distribution of bacteria in many of the other fetal organs, no reaction was visible except in the liver about the vessels containing the organisms. There was also some accumulation of histiocytes. In a note mention is made of five more cases of fetal bacteremia occurring in fetuses of three to five months. Bacteria were found in the bronchi and gastro-intestinal tract of one fetus of only three months' development, showing that even in this early state infected amniotic water can be aspirated or swallowed.

A. J. KOBAK.

AMNIOTIC ADHESIONS. J. OLOW, Beitr. z. path. Anat. u. z. allg. Path. **79**:27, 1927.

On the basis of two cases studied in detail, Olow concludes that amniotic adhesions result from incomplete dehiscence of the ectodermal epithelium of the embryoblast in the formation of the amniotic cavity. A multilocular instead of a unilocular cavity is thus formed. During further development the septums are transformed into strandlike and membranous adhesions.

O. T. SCHULTZ.

A Rare Malformation of the Tricuspid Valve. A. Arnstein, Virchows Arch. f. path. Anat. **266**:247, 1927.

A case of congenital malformation of the tricuspid valve (Ebstein's disease) is described. There was dilatation of the right auricle, contraction of the right ventricle with poor development of its wall, and open foramen ovale. Clinically, systolic and diastolic murmurs, thrills, cyanosis and polycythemia were observed.

B. R. Lovett.

Malformation of the Left Ventricle. H. O. Kleine, Virchows Arch f. path. Anat. **267**:284, 1928.

After reviewing the literature, Kleine describes his case, in which a band was found resembling one of the chordae tendineae extending from the valve of the foramen ovale to the free border of the mitral valve between the two leaflets. It appeared to be a prolongation of the flap covering the foramen ovale. There were also three, instead of two, pulmonary veins.

B. R. Lovett.

Malformations of the Organs of Respiration. F. Paul, Virchows Arch. f. path. Anat. **267**:295, 1928.

Three instances of malformations are described. In the first, the left lung was lacking and the pleural cavity was entirely filled by the pericardium and right lung. A rudimentary lung was attached to the esophagus. In the second case, an artery branched off from the aorta just above the diaphragm, and entered the lower lobe of the left lung. Its branches anastomosed with the left pulmonary artery. Extensive caseous tuberculosis was present, confined to the region supplied with blood from the aorta. The third case, that of a stillborn infant, revealed the upper end of the esophagus ending blindly, and the lower end attached to the trachea at the bifurcation. All three are attributed to a fault in the segmentation process, during the development of the lung from the foregut in early embryonic life.

B. R. Lovett.

An Amniogenous Malformation of the Skull and Brain. F. Fritschek, Virchows Arch. f. path. Anat. **267**:318, 1928.

In a stillborn infant, the calvarium was lacking, and the hemispheres consisted of two small rudimentary nodules. There were adhesions between the placenta and the right hemisphere, and also two bands which caused a split in the face and a deformity of the left arm. "Very little amniotic fluid" was reported at the birth.

B. R. Lovett.

Congenital Nonspecific Pneumonia and Pneumonia from Aspiration in the Birth Passages. H. Hook and K. Katz, Virchows Arch. f. path. Anat. **267**:571, 1928.

In an investigation of stillbirths and infants dying in the first few days of life, nonspecific aspiration pneumonia was found to be a frequent cause of death. In seventy-three autopsies, congenital pneumonia was present twenty-two times and pneumonia in the first few days of life fourteen times. The presence of pneumonic foci could be determined in many cases only with the microscope. Amniotic fluid or other constituents of the birth canal were found regularly in the lungs. The pneumonias were of bronchogenic origin, even the congenital cases, due to aspiration of infectious material; there was no evidence of blood infection through the placenta. Histologic examination of the lungs should be made more frequently in these infants, especially in those dying with signs of asphyxia.

B. R. Lovett.

MALFORMATIONS OF EXTRAHEPATIC BILE DUCTS. FRIEDRICH FEYRTER, Virchows Arch. f. path. Anat. **271**:20, 1929.

The author reviews and groups the reports available in the literature; he adds three original observations. Cystic dilatation and atresia may be found together; the malformations are generally multiple. The teratologic termination point is early. The causes are unknown.

ALFRED PLAUT.

ISO-ANTIBODIES IN MOTHER AND FETUS. NILE LIEDBERG, Acta path. et microbiol. Scandinav. **6**:1, 1929.

The blood groups of 200 mothers and their 200 new-born infants were determined. In 116 children the groups were the same as in the mothers; in all children the receptor was qualitatively determined at birth, while the iso-agglutinin was present in only 60. In seven children agglutinins were present which differed from those of the mothers and indicated that a child may develop its own agglutinin during fetal life. Normal hemolysin for sheep corpuscles was transmitted from mother to fetus in only a few instances and whether the group of the child is the same or differs from that of the mother seemed to make no difference. Isohemolysin occurs in the blood of some new-born infants, and the resulting hindrance to agglutination may be avoided by inactivation of the serum which may even increase the agglutinative titer. Intoxications of pregnancy, birth difficulties or icterus neonatorum do not seem to be related to blood grouping.

AUTHOR'S SUMMARY.

FAMILIAL CONGENITAL MACROSOMIA ADIPOSA. T. CHRISTIANSEN, Hospitalstid. **71**:421, 1928.

Christiansen discusses the endocrine disorder designated by this name, seen in the children of two sisters with menstrual anomalies. Of nine children born at term, seven had macrosomia, five dying within the first year. Necropsy revealed adenomas in the suprarenal cortex and eosinophilia in the thymus. Congenital macrosomia is regarded as a suprarenal syndrome belonging to the obese type (Guthrie and Emery), due to a hyperepinephry (Apert), but distinguished by the absence of hirsuties and genital changes and in other ways from the suprarenal syndromes described in the literature to date.

[ARCH. PATH.]

Diseases of the New-Born

CAN INTRACRANIAL BIRTH INJURIES BE PREVENTED? HUGO EHRENFEST, J. A. M. A. **92**:97 (Jan. 12) 1929.

The author deals with birth injuries from the standpoint of the obstetrician. A distinction is made between physiologic traumatization and true pathologic birth injury. In the first class should be placed all those anatomic observations and immediate clinical manifestations which in general express a sort of contusion or contusions of the brain and which, as a rule, disappear shortly with no later consequences. In the second class, if death does not occur, later consequences may frequently be expected, as they are caused by hemorrhage and injury to nerve tissue. A point well emphasized is that serious injuries responsible for immediate death or later disability are not inflicted solely during labor itself, but may result when infants are improperly managed physiologically or are slightly traumatized. Serious harm will be obviated if the seemingly asphyxiated child is considered as probably intracranially traumatized.

BONAR, Salt Lake City.

PRENATAL PREVENTION OF POTENTIAL HEMORRHAGE DISEASE OF THE NEW-BORN. I. NEWTON KUGELMASS and JOHN E. TRITSCH, J. A. M. A. **92**:531 (Feb. 16) 1929.

Study of the clotting components of the blood during pregnancy in a woman who had lost three, and possibly four, infants from melena neonatorum showed

prothrombin deficiency analogous to that observed in true melena neonatorum. Institution of nutritional therapy throughout pregnancy produced and maintained normal maternal blood before birth; the fifth pregnancy resulted in the birth of a nonbleeding infant. The possible value of prenatal treatment in bringing about physiologic perfection in the new-born is apparent. BONAR, Salt Lake City.

HEMORRHAGIC CONDITIONS OF THE NEW-BORN. HARRY S. SNYDERMAN, M. J. & Rec. **129**:244 (March 6) 1929.

The clinical as well as the pathologic data presented in the literature show general agreement as to the enormous frequency of cerebral injury at birth. Wohwill found that cerebral trauma at birth causes a loss of human life so great that it may be considered as one of the most widely spread diseases. The mortality is one of the greatest. The use of early and correctly applied forceps does not increase the danger of intracranial hemorrhage, but prolonged labor, causing extreme intracranial venous stasis, is a big causative factor; this is especially true when forceps are used as a last resort. Early lumbar puncture on the infant is a diagnostic aid and, in intracranial hemorrhage, a most important part of the active treatment. It should be repeated every twelve or twenty-four hours, depending on the severity of the case. Coagulation time and bleeding time should be ascertained as a routine on every new-born infant, and whole blood should be given to every one that shows a prolonged coagulation or bleeding time. The blood should be given until improvement is seen. By this means, future symptoms and fatalities may be eliminated.

WILLIAMSON, New Orleans.

STILLBIRTHS AND NEONATAL DEATHS IN 1,960 CONSECUTIVE PRIVATE CASES. JAMES KNIGHT QUIGLEY, New York State J. Med. **29**:319 (March 15) 1929.

The rate of stillbirths was found to be 2.34 per cent, and the rate of neonatal deaths 1.17 per cent, making a gross mortality of 3.51. Of stillbirths, eleven were due to accidents to the cord, ten to dystocia and nine to toxemia of pregnancy. Hemorrhagic disease was the cause of five neonatal deaths, toxemia of four and dystocia of three deaths.

AIKMAN, Rochester, N. Y.

SIMPLE ICTERUS OF THE NEW-BORN. P. LEREBOULLET, Progrès méd. **30**:1274 (July 27) 1929.

In the fetus at the time of birth, there is an existing increase in bilirubin because the only path of excretion is through the placenta. Tying the cord at birth causes icterus, because this usual path of excretion is suddenly blocked, and this plus the many causes of hemolysis of the blood existing at this period is sufficient to cause hypercholemia, or visible icterus. The intestines are not yet adapted to the excretion of this excess bile, and usually the liver and kidneys are not as yet functioning properly. In a few days the liver and kidneys begin to function normally; the excess of bile is removed from the intestinal tract; the skin clears and the amount of bilirubin in the blood falls to a normal value. Only if the icterus persists or is intensified can one consider it as a pathologic process.

SANFORD, Chicago.

SCLERODERMA IN THE NEW-BORN. C. LUZ, Arch. de Pediat., Rio de Janiero **9**:292 (June) 1929.

The case is illustrated with photomicrographs from the nodules showing the proliferation of fibroblasts, with mononuclear infiltration and the formation of giant cells. Histologic examination offers the only means of sure diagnosis.

SANFORD, Chicago.

RETICULOCYTES IN EMBRYOS AND THE NEW-BORN. R. JÜRGENS, Virchows Arch. f. path. Anat. **266**:676, 1928.

The blood of 300 mouse embryos was investigated. Two developmental series of red cells could be distinguished, the megaloblastic and the normoblastic. In young embryos, all erythroblastic cells contained vitally stained granulations, and a definite formation and growth of substantia granulofilamentosa could be determined, similar for both series. In later embryonic life, the number of reticulocytes diminished progressively with the disappearance of the cell nuclei until birth. New-born mice had an average of from 60 to 70 per cent of reticulocytes, falling to from 30 to 40 per cent in the first hours of life, and to from 0.5 to 2 per cent after a few weeks. In human infants the percentage was 7 at birth, 2 at 10 days and 0.7 at 6 weeks. In premature infants, the number was much greater, from 11 to 30 per cent at birth. The substantia granulofilamentosa represents a constant morphologic stage in the process of normal development of all hemoglobin containing blood cells in man and in animals. This substance is a remainder of the original blood cell protoplasm, and diminishes as pyknosis and karolysis of the nucleus occur, until it disappears entirely in the mature cell.

B. R. LOVETT.

GLANDERS-LIKE PYEMIA IN A BREAST-FED NEW-BORN CHILD. ALFRED PLAUT, Virchows Arch. f. path. Anat. **270**:672, 1929.

A normally delivered, mature infant of a healthy primipara became sick at the end of the first week. The temperature was 104 F., with green liquid stools, swelling of the abdomen and finally vomiting. Death occurred on the eighteenth day of life. The liver and spleen were found studded with irregularly distributed, spherical, well outlined, yellowish-green foci, averaging in size between that of a rice grain and that of a pepper seed. One such focus was found in one kidney and larger, less regular nodules in a lung; confluent foci diffusely involved the cecum and appendix; necrosing colitis was found in the colon ascendens; there was diffuse serofibrinous peritonitis and pleuritis; the abdominal lymph nodes were partly supplanted by such foci; the lymph nodes at the porta hepatis were intact; the umbilical vessels were partly thrombosed, but otherwise were unchanged. The microscopic examination showed necroses with thick masses of bacilli at the periphery. The bacilli were gram-negative, short, straight or banana-shaped and resistant to any staining, only the poles and the periphery taking the strain well. Their dense, inextricable masses closely imitated mycelium. They filled the blood vessels. The reaction of the tissue surrounding the foci extended through a narrow zone only. The diffuse colitis was the result of confluent hematogenous foci. The foci in the lung were larger and less regular in shape; the bronchi were secondarily affected. The thymus and suprarenal glands were small. The skull and the organs of the neck were not examined.

Cultures from heart blood, exudates and spleen yielded *Bacterium coli*, nonpathogenic for guinea-pigs (fed and injected). The colon bacillus was not identical with the organism in the lesions. Incubation of a piece from liver in broth for ten hours did not lead to an increase in the number of bacilli within the tissue.

The source of the infection, the point of its entry and the character of the organism are unknown. The main seat of infection was the colon. Four photographs demonstrate the similarity with glanders.

ALFRED PLAUT.

CYANOSIS OF THE FACE AND ARMS IN THE NEWLY BORN. J. SAHLER, Wien. klin. Wchnschr. **42**:622 (May 2) 1929.

The author observed several cases of transient cyanosis of the face, arms and upper part of the body in the newly born. The fluoroscope revealed a broad shadow in the region of the right auricle. In the absence of necropsy, the author assumes the presence of some obstruction in the superior vena cava.

CLAUSEN, Rochester, N. Y.

ISOHEMAGGLUTINATION IN MOTHERS AND NEW-BORN CHILDREN. P. MORVILLE, Acta path. et microbiol. Scandinav. **6**:39, 1929.

The isohemagglutinative groups were determined for 500 mothers and their 518 children, of whom 63.1 per cent belong to the same blood group as the mother, and 61.2 per cent had iso-agglutinin present at birth. When mother and child belonged to the same group iso-agglutinin was more frequently found at birth, in 95 per cent when the group was O as contrasted with about 50 per cent when the group was A or B. When the group of the child differed from that of the mother iso-agglutinin was present in the child at birth only when one of them was in group O, and a child in group O with a mother in group A or B does not have the agglutinin combination a + b, but has only the agglutinin which is present in the mother. The conclusions from these studies of children at birth and at different ages are that iso-agglutinin passes from the mother's blood to the fetal blood in every instance but is often removed by the child's corpuscles, that the agglutinin present at birth is not the child's own, that the child's own agglutinin is in most cases developed at the end of four months but cannot always be expected in less than one year, and that the receptor (agglutinogen) is always present at birth though possibly weak and not easily determined. Certain paradoxic cases are described. Agglutinin and receptor are regarded as related properties due not to different, mutually independent heredity-factors, but to various hereditarily regulated stages of the same factor, and on the basis of this theory the group characteristics become an expression of genuine immunization. Experimental support is considered essential.

ETHEL B. PERRY.

Acute Infections

VARICELLA COMPLICATED BY ACUTE NEPHRITIS: REPORT OF A CASE ASSOCIATED WITH STREPTOCOCCAL INFECTION OF THE TONSILS. E. RANKIN DENNY and B. M. BAKER, JR., Bull. Johns Hopkins Hosp. **44**:201, 1929.

A case of focal glomerular nephritis occurring early in the course of hemorrhagic varicella is reported. The onset of the nephritis, and the recovery from this complication paralleled the course of a complicating acute tonsillitis due to hemolytic streptococci, of the B type. The organisms isolated from the tonsils and urine had common cultural characteristics. During the acute stage of the nephritis, hemolytic streptococci of B type were found in the urine, while after recovery from the nephritis they disappeared both from the throat and from the urine. It is suggested that the acute hemorrhagic nephritis in this case was associated not with hemorrhagic varicella but with the streptococcal infection.

AUTHORS' SUMMARY.

THE INCUBATION PERIOD OF POLIOMYELITIS. W. LLOYD AYCOCK and ELIOT H. LUTHER, J. Prev. Med. **3**:103, 1929.

Data bearing on the incubation period of poliomyelitis have been collected from the following sources: milk-borne outbreaks; cases following tonsillectomy; isolated groups of cases in the same locality where contact could not be traced; cases in which a single known contact occurred; certain instances of multiple cases in families in which the individuals had separated before the onset of the disease; and an analysis of all cases observed in 1928 in Massachusetts, with known contact, in which an interval of separation had occurred prior to onset. In all cases in which the time of exposure can be set within narrow limits the apparent incubation falls within a period of from six to twenty days. In all cases in which the last exposure occurred less than six days preceding onset of the secondary case, the duration of exposure is such that the incubation period could likewise have fallen within these limits. In none of the observations reported in this paper was the incubation period necessarily shorter than six days. In some of these observations there is evidence that the infectious period of the disease may extend

from the fourteenth day preceding the onset of symptoms to at least the fifth day of the disease. The incubation period observed in the experimental disease in monkeys following inoculation of fully active virus was most often six or seven days, but varied from four to fifteen days. Longer incubation periods were observed following inoculation of modified virus.

AUTHORS' SUMMARY.

THE RÔLE OF THE VACCINATION DRESSING IN THE PRODUCTION OF POST-VACCINAL TETANUS. C. ARMSTRONG, Pub. Health Rep. **44**:1871 (Aug. 2) 1929.

Among 116 investigated cases of tetanus following vaccination, it was found that in all the condition had developed following primary "takes" which had been covered by some type of dressing strapped to the site of vaccination. It is believed that an accumulation of broken down material retained by the dressing at the vaccination site, wherein tetanus organisms may become buried and thus find anaerobic conditions, is the essential condition without which postvaccinal tetanus will not develop under natural conditions.

SANFORD, Chicago.

MENINGOCOCCUS MENINGITIS AND MEASURES FOR ITS CONTROL. G. W. McCOY, Pub. Health Rep. **44**:1595 (July 5) 1929.

During the prevalance of an infection, the carriers are numerous. In a recent study made in Detroit it was found that 46 per cent of household contacts were carriers while 6 per cent of unexposed persons showed meningococci in the nasopharynx. In most carriers the condition clears up in a few days, regardless of what is done. It remains to be shown that the process of recovery from the carrier condition can be hastened by any means now available.

SANFORD, Chicago.

THE STUDY OF ONE HUNDRED DEATHS FROM DIPHTHERIA IN SOUTH CAROLINA DURING THE YEARS 1926-1927. JAMES A. HAYNE, South. M. J. **22**:617 (July) **1929**.

In South Carolina, antitoxin is usually administered to all patients in whom diphtheria is either suspected or diagnosed. The death rate of the disease seems not to change.

Antitoxin must be used to reduce the present death rate. It must be administered before the child has reached school age, preferably to children between the ages of 1 and 3 years.

The author believes that a campaign of education must be carried out to make mothers recognize that any sore throat in a child should have the attention of a physician, and that delay is extremely fatal. Large doses of diphtheria antitoxin do not prevent the death of children after seventy-two hours of the disease.

To be effective, diphtheria antitoxin must be administered in an initial dose of at least 10,000 units, or 20,000 units if the case is malignant. Repeated doses do not seem to have any effect on the disease.

In apparently moribund patients, the procedure of Dr. Park, to give antistreptococci serum along with diphtheria antitoxin is recommended.

SCHLUTZ, Minneapolis.

RHEUMATIC FEVER AND TONSILLITIS. J. TERTIUS CLARKE, Brit. J. Child. Dis. **26**:99 (April-June) 1929.

The author's observations during thirty years in Malaya, as well as the reports of numerous other physicians, lead him to conclude that rheumatic fever is absent from the tropics. Casting about for a probable explanation of this fact, he offers the hypothesis that the disease is insect-borne. The insect that is suggested as the carrier is the rat-flea, *Ceratophyllus fasciatus*, found only in temperate climates.

As substantiation of his theory he offers the fact that rheumatic fever is usually found among the poorer classes who dwell in damp and poorly ventilated houses and that rats infest such places.

The claims that the tonsils are the portal of entry of the rheumatic infection have not been definitely proved. About half of the children suffering with rheumatism, according to numerous observers, showed no signs or symptoms of tonsillitis at any time. Furthermore, rheumatic fever is not connected with sore throats caused by overcrowding and poor ventilation, such as is found in the large public schools, but there seems to be an association between rheumatic fever and the sore throat derived from bad drains.

LANGMANN, New York.

THE SCHICK REACTION AND CIRCULATING ANTITOXIN. A. T. GLENNY and HILDA WADDINGTON, J. Path. & Bact. **32**:275, 1929.

Tolerance for diphtheria toxin may be determined by the intracutaneous injection of multiples of the Schick dose. Large reactions may be avoided by the use of toxins so chosen that the specific toxicity of the dilutions used is the same as that of the routine Schick dilution but the combining power is greater. A concentration of antitoxin in the blood 1/250 unit per cubic centimeter of serum corresponds to the Schick negative level in guinea-pigs. In passively immunized guinea-pigs, this correspondence is not reached until equilibrium is reached between the circulation and tissues many hours after the injection of serum.

AUTHORS' SUMMARY.

PROLONGED PNEUMOCOCCUS SEPTICEMIA SUGGESTIVE OF MALARIA. G. BOULANGER-PILET and A. GONDAL, Bull. Soc. de pédiat. de Paris **27**:237 (May) 1929.

A boy, aged 2½ years, suddenly developed fever of the septic type, with chills and sweats suggestive of malaria. The fever lasted for four and one-half months. At no time was there pharyngitis, bronchitis, pneumonia, abdominal symptoms or enlargement of the spleen. From the twenty-third to the eighty-sixth day morbilliform and purpuric lesions of the skin appeared. From one of the lesions and from the blood pneumococcus type I was cultivated. No form of therapy (antipneumococcus serum, vaccines, stovarsol, sodium salicylate and injections of the mother's blood) had the slightest effect on the illness. Spontaneous recovery was complete.

CLAUSEN, Rochester, N. Y.

WHOOPING COUGH. THORVALD MADSEN, Rev. franç. de pédiat. **5**:145 (April) 1929.

Whooping cough, unlike many other diseases, does not show a definite seasonal incidence. The mortality rate, however, is always greater in the spring months because of the greater frequency of bronchopneumonia as a complication. Early diagnosis is of great importance in controlling epidemics. In achieving this, use should be made of cultural methods of obtaining the Bordet-Gengou bacillus. By the use of special mediums and the exposure of the plates to the cough of the patient, the author states that positive cultures are obtained in 75 per cent of the cases during the first week of the disease, i.e., during the period of catarrh; 57 per cent during the first week of the cough; 61 per cent during the second, 45 per cent during the third, 40.5 per cent during the fourth and 9 per cent during the fifth week. These figures are based on a study of 914 cases. The author favors the use of vaccine in treatment and prevention, although he is not sure whether its action is specific or whether the results are due purely and simply to the protein contained in the bacteria.

LESLIE, Evanston, Ill.

THE WHITE CELLS IN MEASLES. SOPHIE OLECHNOWIEZ, Rev. franç. de pédiat. **5**:209 (April) 1929.

In a study of the white cells of the blood in thirty-two cases of measles, the following characteristics were observed: (1) period of incubation: leukocytosis, eosinophilia, shift of neutrophils to the left; (2) period of invasion: shift of neutrophils to the left, diminution or lack of eosinophils, leukopenia; (3) period of eruption: with good prognosis, leukopenia; shift of neutrophils to the left; with bad prognosis, leukocytosis; lymphocytosis; decrease in monocytes and eosinophils; (4) posteruptive period: leukocytes slightly increased, lymphocytes slightly increased or normal, eosinophils and monocytes increased.

LESLIE, Evanston, Ill.

IMMUNIZATION AGAINST CHICKENPOX. F. BENINI, Riv. di clin. pediat. **26**:824, 1926.

Benini gives his experiences with vaccination against chickenpox. He employed vaccination in forty cases, in twenty-seven using the scarification method and in thirteen intradermal inoculation with the lymph. He concludes that vaccination against chickenpox, if carried out with great care, is absolutely harmless. Prophylactic vaccination makes it possible to limit the spread of the disease. The best results are secured by employing the intradermal route. If chickenpox were always the mild disease that it is commonly, vaccination might be said to have chiefly an academic or scientific interest, but the fact is that the disease is not always benign but often takes on a nature dangerous to life, particularly in hospitals and gouttes de lait in which the patients are in a condition of lessened resistance.

O. T. SCHULTZ.

POSTVACCINAL ENCEPHALOMYELITIS. P. SCHÜRMANN, Beitr. z. path. Anat. u. z. allg. Path. **79**:409, 1928.

Although postvaccinal encephalomyelitis has shown a decided increase since 1922 in England and Holland, where the condition has been carefully studied histologically, the author claims that there are no previous reports of histologic studies in the German literature. The two cases studied by him occurred in children, aged 8 years and 18 months, respectively. The characteristic change noted by him was a zone of demyelinization about the dilated veins, usually at the junction of white and gray matter. Proliferation of glia was also noted. The changes occurred in both brain and cord. In the older child, in whom the vaccination was complicated by numerous furuncles in the axillae and on other parts of the body, there was infiltration by lymphocytes and large mononuclear cells about some of the veins, in addition to the more characteristic demyelinization. In his discussion of the nature of the process, the author does not accept the view of Luksch that the involvement of the nervous system is directly due to the vaccine virus. Perhaps the latter prepares the ground in susceptible persons for changes which are the result of nonspecific toxins. Schürmann holds the encephalomyelitis following vaccination to be identical histologically with that which may follow measles.

O. T. SCHULTZ.

CONGENITAL INFECTIONS. EUGEN STRANSKY, Monatschr. f. Kinderh. **43**:193 (May) 1929.

This article should interest all pediatricians. It is a thorough review of all the literature in the last decade in which there are reports of congenital infections. The author concludes that there is definite evidence of the transmission of measles, scarlet fever, typhoid and paratyphoid, anthrax, pneumonia, influenza, malaria, tuberculosis and probably leprosy. The evidence is insufficient as yet in regard to pertussis and epidemic encephalitis. Of the diseases caused by *Spirilla,* relapsing fever seems definitely to be transmitted. Of course, in the matter of intra-uterine infections, syphilis is in a class by itself.

GERSTLEY, Chicago.

Internal Diseases

BRONCHOSCOPIC FINDINGS IN LOBAR PNEUMONIA: A PRELIMINARY NOTE. P. N. CORYLLOS, Am. J. M. Sc. **178**:8 (July) 1929.

Coryllos produced experimental pneumonia in dogs by intrabronchial insufflation of eighteen hour old cultures in broth of pneumococcus type I, concentrated ten times by centrifugation. Almost constantly a lobar pneumonia confined in the insufflated lung was obtained. Bronchoscopic examination showed that the bronchus of the affected lung or lobe did not breathe. Bronchoscopic aspiration yielded variable amounts of brownish viscid fluid from the corresponding lung. After aspiration the lung often became somewhat aerated, but the investigators were unable to save the animals as the pneumonic process continued after variable periods of relief.

Bronchoscopic examinations were made in nine cases of pneumonia; the technic of bronchoscopy is described, and reports of the nine cases are given. It was shown that in the nine cases the bronchus corresponding to the consolidated area was occluded and circulation of air was shut off, supporting the hypothesis that lobar atelectasis and lobar pneumonia are due to the same mechanism, namely, the occlusion of the bronchus.

Table I gives an analysis of the patients with pneumonia on whom bronchoscopy was done. The mortality rate was 33.3 per cent. Table II shows an analysis of fourteen patients with pneumonia who were used as controls, showing a mortality rate of 72 per cent. No conclusion can be drawn for the reason that the number of patients on whom bronchoscopy was performed was small, and also that the cases were the less toxic ones.

Coryllos demonstrated that bronchoscopic examination of patients with pneumonia does not cause any shock and that all of the patients feel more or less relieved in proportion to the amount of the exudate aspirated or spontaneously expectorated after bronchoscopy. He expresses no opinion as to the possibility of therapeutic influence of bronchoscopy in pneumonia. He states that the pathologic observations seem to support experimental facts on which the theory was based that lobar pneumonia starts as a pneumococcic atelectasis and the affected lobes in lobar pneumonia are smaller than the healthy ones.

HENSKE, Omaha.

INFECTIONS OF THE UPPER RESPIRATORY TRACT AND MIDDLE EAR. JOHN H. FISHER, J. Infect. Dis. **44**:33, 1929.

The pathogenicity of the organisms isolated from fifteen cases of infection of the middle ear in man was tested in rabbits by intranasal inoculations. The nasal passages of the rabbits were previously swabbed with a 50 per cent aqueous solution of phenol. Eleven of these rabbits died, and in each case acute purulent paranasal sinusitis and acute otitis media were found. From these lesions, in each instance, an organism similar to the type inoculated was recovered. Associated lesions, in some of the rabbits, were acute pleuritis and empyema, lobular pneumonia, abscesses of the lung, acute pericarditis and septicemia. From these lesions, in each case, organisms similar to those inoculated intranasally were recovered. The experiments were controlled by two groups of rabbits, one group receiving culture only, intranasally, the other receiving swabbing only. None of the rabbits of these two groups died. Some factor which lowers the resistance of the nasal mucosa is necessary for the infection of the upper respiratory tract and middle ear. In twelve untreated normal control rabbits there was no evidence of otitis media.

It is thought that the use of 50 per cent phenol as a means of reducing resistance of tissue may prove of value in the experimental infection of animals.

Fifty cases of acute infection of the middle ear in man were studied bacteriologically. *Streptococcus hemolyticus* was the exciting organism most frequently found, while staphylococcus and pneumococcus were next.

The evidence indicates that otitis media is not blood-borne, but develops by direct extension from an infection of the upper respiratory tract.

AUTHOR'S SUMMARY.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. JACKSON W. LANDHAM, South. M. J. **22**:639 (July) 1929.

There seems to be some unknown etiologic factor that produces a stenosis of the pylorus at or before birth.

The differential diagnosis can be made easily by fluoroscopic study of the stomach.

The treatment is surgical in all cases of congenital pyloristenosis, the Rammstedt or some of its modifications being the operation of choice.

SCHLUTZ, Minneapolis.

ADENOMA OF THE KIDNEY. H. L. KRETSCHMER and C. DOEHRING, Surg. Gynec. Obst. **48**:629, 1929.

A thick bluish-white membrane, from 0.5 to 1 mm., encapsulated a tumor, 12 by 15 by 15.5 cm., weighing 760 Gm., that arose from the right kidney, leaving a small residual portion of the kidney which was located on the upper pole of the tumor. This mass, which was of uniform consistency, was composed of cuboidal or hexagonal cells in more or less alveolar arrangement. The nuclei of the cells were large and contained abundant chromatin. In the literature sixteen similar cases were found, the youngest in a girl, 11 months of age. The genesis is ascribed to rests of renal tubules, error in development, remnants of the wolffian body, or cells which possibly were destined to form kidney substance but were early diverted to the formation of a tumor. There has been no recurrence four years after the removal of the adenoma in the case described.

RICHARD A. LIFVENDAHL.

INFANTILE KALA-AZAR: A CASE CURED AT ALEXANDRIA BY A NEW METHOD. ANGÉLIQUE PANAYOTATOU, Brit. J. Child. Dis. **26**:112 (April-June) 1929.

A native boy of Alexandria, Egypt, aged 2½ years, had been ill for six months before admission, with gastro-intestinal disturbances, irregular fever and progressive emaciation. On physical examination he showed marked anemia (red blood cells, 3,000,000; hemoglobin, 45 per cent; white blood cells, 3,000; polymorphonuclears, 48 per cent; lymphocytes, 36 per cent; large mononuclears, 12 per cent; transitionals, 4 per cent), a large abdomen and a large spleen. On splenic puncture, Leishman-Donovan bodies were found. No parasites were found in the peripheral circulation.

A new method of treatment was tried; i. e., instead of giving antimony and potassium tartrate intravenously it was given by the intestinal route. Four cubic centimeters (0.01 Gm. or 1 cg.) of a weak solution, 0.25 Gm. in 100 cc., was given every other day. Slight improvement was noted after the fifth injection; the dose was then increased to 6 cc. (0.015 Gm.) for four injections, then to 0.02 and 0.025 Gm. In three months, the patient received 0.5 Gm. of antimony and potassium tartrate. He was discharged cured, and when seen four months after discharge was in good health.

LANGMANN, New York.

X-RAY DIAGNOSIS OF MITRAL STENOSIS. HAROLD COOKSON, Lancet **1**:1344 (June 29) 1929.

In forty cases of rheumatic heart disease "in which mitral stenosis was almost certain from clinical examination," the orthodiagraph showed the following changes which the author is inclined to term typical because of the frequency of their occurrence: (1) in 72.5 per cent, prominence of the pulmonary artery and dilatation of the left auricle, and (2) in a further 7.5 per cent, prominence of the pulmonary artery only.

LANGMANN, New York.

A Mediastinal Teratoma in a Young Infant. A. J. Poynton, Proc. Roy. Soc. Med. **22**:635 (March) 1929.

An infant, aged 4 months, with clinical evidence of a cystic tumor in the upper and anterior mediastinum, died at the age of 9 months. At autopsy, the tumor was found to be a teratoma. The occurrence of such tumors in children is briefly discussed in the article. There is also a full clinical and pathologic description of the present case in the report which is accompanied by a roentgenogram of the thorax and a photograph of it at autopsy.

Williamson, New Orleans.

A Clinical Method of Estimating Cardiac Efficiency in Children and the Work of a Rheumatic Supervisory Center. Gerard, Proc. Roy. Soc. Med. **21**:893 (May) 1929.

The article describes the work carried on at a Rheumatism Supervisory Center. The means for estimating cardiac efficiency were simple. The following six factors were taken: (1) pulse rate while reclining; (2) pulse rate while standing; (3) increase in pulse rate on standing; (4) increase in pulse rate after exertion; (5) time for pulse to return to normal, and (6) difference in blood pressure on lying and standing. The report is accompanied by a number of cardiac efficiency tables based on a large number of cases at the center.

Williamson, New Orleans.

Rupture of Heart from Abscess. G. H. Stevenson and A. J. Marshall, Glasgow M. J. **110**:337, 1928.

A boy, aged 9 years, died without warning from the rupture of the left ventricle through a myocardial abscess which had formed in the course of a pyemia of traumatic origin.

[Arch. Path.]

Bronchopneumonia in Infants. H. Grenet and L. Guillemot, Bull. Soc. de pédiat. de Paris **27**:89 (Jan.) 1929.

The authors give statistics regarding 212 cases of bronchopneumonia in infants observed at the Bretonneau Hospital from October, 1927, to July, 1928. Of these, 117 died (16 within forty-eight hours after admission to the hospital) and 95 were cured, a mortality rate of 55.2 per cent. Only 2 of 31 patients with primary bronchopneumonia who were treated with two or three injections of vaccine (the exact nature of which is not mentioned) recovered. Eleven patients (8 with cases secondary to measles and 3 primary) treated with two or three injections of vaccine and 120,000 units of diphtheria antitoxin in four days died. Of 154 patients who received a complete course of Duchon's vaccine, 93 recovered and 61 died, a mortality rate of 39.6 per cent. Twenty-three of 88 patients who received the vaccine and intensive treatment with diphtheria antitoxin died, a mortality rate of 26.1 per cent. The mortality rate for infants under the age of 1 year who received the vaccine was about 50 per cent. Fifteen of 21 pharyngeal cultures from patients with bronchopneumonia following measles showed Klebs-Löffler bacilli. The authors believe that the use of Duchon's vaccine in bronchopneumonia reduces the mortality rate; they also believe that in a hospital in which diphtheria is present the vaccine should be followed by the use of diphtheria antitoxin.

Benjamin, Montreal.

Four Cases of Infection of the Urinary Tract in Infants Treated with the Colon Bacillus Antiserum of Vincent. Jean Dayras and Robert Bernheim, Bull. Soc. de pédiat. de Paris **27**:97 (Jan. 22) 1929.

The authors report four cases as follows:

1. A girl, aged 26 months, who had persistent pyuria in spite of every treatment over a period of two years, was given three injections of antiserum without any improvement. Ureteral catheterization showed the pus to be of renal origin.

2. A girl, aged 7 months, with marked pyuria, was given seven injections of 5 cc. each. The urine became free from pus. The patient later developed varicella and measles, and the pus in the urine returned.

3. A girl, aged 7 months, whose urine was loaded with albumin and pus, was given four injections. She began to improve, but became temporarily worse, during which time she contracted varicella. The urine became free from albumin and pus.

4. A girl, aged 16 months, with marked pyuria, was given colon vaccine by mouth. The temperature fell to normal in two days, but the pain and pyuria continued as previously. She was then given three injections of antiserum, and the urine cleared of pus in four days.

The authors consider two patients cured, one improved and one unimproved. In the one who was unimproved, they feel that they might have had a better result if they had pushed the antiserum treatment. All four patients had marked serum reactions.

BENJAMIN, Montreal.

RHEUMATIC PERICARDITIS AND PANCARDITIS OF BOUILLAUD'S DISEASE. P. NOBECOURT and BOULANGER-PILET, Bull. Soc. de pédiat. de Paris, May, 1929, no. 5, p. 2110.

Of thirteen cases of pericarditis observed in recent years by the authors, eight have been of a mild and five of a severe type. In no case was pericarditis the only cardiac lesion, and in none did the serious outcome depend on it alone.

CLAUSEN, Rochester, N. Y.

PERICARDITIS AND SEPTICEMIAS DUE TO THE STREPTOCOCCUS. J. HUTINEL, LEBÉE and FÈVRE, Bull. Soc. de pédiat. de Paris, May, 1929, no. 5, p. 2160.

The authors review three cases of purulent pericarditis observed by others and report one of their own. Each case began with septicemia; the type of streptococcus varied—*S. erysipelatis, S. hemolyticus, S. viridans.* Multiple localization occurred: pleural, pericardial and endocardial. Nevertheless, every patient recovered. The authors are inclined to attribute the recovery to the beneficial effects of the spontaneous formation of a fixation abscess.

CLAUSEN, Rochester, N. Y.

PERSISTENCE OF HEMATOLOGIC SIGNS AFTER CLINICAL CURE IN THE SYNDROME OF WERLHOF. NOBÉCOURT and KAPLAN, Bull. Soc. de pédiat. de Paris, May, 1929, no. 5, p. 259.

In a typical case of thrombopenic purpura, the authors have described the disappearance of symptoms and the return of the bleeding time to normal before the platelets had become normal in number. They do not mention the method used in counting the platelets, and the number given at the time of severe symptoms is 81,000.

CLAUSEN, Rochester, N. Y.

INTERSTITIAL MYOCARDITIS. A. MAZZOO, Pediatria **37**:768 (July 15) 1929.

A girl, aged 2 years, was brought to the hospital with edema of the face and legs. The mother had died of postscarlatinal nephritis. The patient had had measles four months previously.

The patient had been sick for only three days, during which there had been a notable diminution in the urinary output.

The physical examination disclosed a marked left cardiac enlargement and albuminuria.

The lungs were normal; the reaction to tuberculin was negative.

Death ensued in a few days.

At autopsy, a marked dilatation of the left ventricle with many old parietal thrombi, a slight dilatation and hypertrophy of the right ventricle and a small anemic infarct in the left kidney, with chronic passive congestion of all the viscera, were found. The thymus weighed 15 Gm.

Histologic examination disclosed, in addition to fat in the myocardium, many round cells infiltrating the spaces between the muscle fibers which seemed to be compressed. The cells were practically all lymphocytes, and were found also in a few scattered areas of the endocardium.

The author lays stress on the sudden and rapidly progressive onset of the symptoms, and the absence of a status lymphaticus.

SALA, New York.

PERNICIOUS ANEMIA AND APLASTIC ANEMIA IN INFANCY. JUAN ORRICO, Arch. latino-am. de pediat. **22**:125 (March) 1929.

These forms of anemia are exceedingly rare in childhood and especially in infancy. The author reviews the cases reported in the literature and reports two additional cases, one in an infant aged 2½ years, and one in an infant aged 2 years and 4 months.

There was no tuberculosis or syphilis in either case.

The blood in the first case showed oligocythemia, diminution of platelets, leukopenia, a relative lymphocytosis and the presence of normoblasts, megalocytes, hyperchromatic cells and megaloblasts.

In the second case there was a great diminution of the red cells, intense leukopenia and a hemoglobin index under 1.

The leukocyte formula was characterized by relatively high lymphocytosis. There was no erythroblastic or myeloid reaction. A hemorrhagic diathesis was present, with manifestations of purpura.

SCHLUTZ, Minneapolis.

THREE CASES OF LEUKEMIA IN INFANCY. A. PEREZ ARA, Bol. Soc. cubana de pediat. **1**:198 (April) 1929.

Three infants with leukemia in whom the white counts were 90,000, 190,000 and 100,000, respectively, were treated by injections of blood and radiotherapy to the splenic region. The condition was apparently improved and the children were alive after several years. Perez Ara discusses the etiology and hematology of the leukemias and the various forms of treatment. He believes that blood transfusion and treatment with radium or radioactive substances are specific.

SANFORD, Chicago.

PYELITIS OF INFANCY. E. TORROELLA, Bol. Soc. cubana de pediat. **6**:324 (June) 1929.

Torroella reviews the subject of pyelitis in infancy. For treatment he prefers the initial giving of a purgative, followed by doses of methenamine. He uses alkalis rarely. Vaccines may be attempted if methenamine fails.

SANFORD, Chicago.

PRIMARY, GENERALIZED ROUND CELL SARCOMA OF THE LYMPH GLANDS. E. HERZOG, Centralbl. f. allg. Path. u. path. Anat. **44**:129, 1928.

A girl, aged 15, entered the hospital because of painless, generalized enlargement of the lymph glands of five weeks' duration. Two weeks later a small tumor developed beneath the skin of the right third intercostal space, and eight days later an abscess of the palate. The lymph glands were the size of a plum; the Wassermann reaction of the blood was negative, and the blood picture was typical of a secondary anemia. A clinical diagnosis was made of aleukemic leukemia. At autopsy there was a tumor-like systemic involvement of all lymph glands, and there were small metastases in the pericardium, trachea, sternum, skin of the right shoulder and marrow of the femur. Microscopically, the structure of

the lymph glands was distorted by many large round or polygonal cells with abundant protoplasm with large vesicular nuclei rich in chromatin and with abundant mitoses. The capsules of the lymph glands generally were thickened but free from infiltrations of tumor cells or small lymphocytes, whereas in the region of the mediastinum and trachea the invasive character of the tumor was evident. The origin of this large round cell sarcoma of the lymph glands was therefore thought to be probably in the mediastinum.

GEORGE RUKSTINAT.

METHOD OF TREATMENT OF DISEASES OF THE VAGINA IN YOUNG GIRLS WITH UNRUPTURED HYMEN. E. LEIBHOLZ, Deutsche med. Wchnschr. **55**:962 (June 7) 1929.

Referring to an article by Calmann, the author recommends the use of a small cystoscope in the treatment for vaginal disease in young girls with unruptured hymen. By the use of this instrument, he is able to apply all forms of medication and to use the cautery without rupturing the intact membrane.

SCHERER, Duluth.

DIAGNOSTIC ERRORS IN DISEASES OF THE LUNG IN CHILDHOOD. W. EWE, Monatschr. f. Kinderh. **43**:233 (May) 1929.

In four cases, tuberculosis was diagnosed by physical observations and roentgen examinations. Reactions to the Pirquet tests were negative. On the basis of these, the author ruled out tuberculosis. All patients made a complete recovery in several weeks. He makes a plea for the more frequent use of the tuberculin skin tests.

GERSTLEY, Chicago.

ACUTE RED ATROPHY OF THE LIVER IN A CHILD. MATZDORFF, Monatschr. f. Kinderh. **43**:262 (May) 1929.

A child, aged 3 years, was admitted to the hospital with symptoms of sepsis, marked icterus, meteorism and ascites, enlarged liver and acholic stools. Autopsy showed acute red atrophy of the liver, which is probably a variation of yellow atrophy. The etiology is unknown, but the condition is probably caused by sepsis.

GERSTLEY, Chicago.

HIRSCHSPRUNG'S SYNDROME AS THE FIRST SIGN OF CONGENITAL MYXEDEMA. J. C. SCHIPPERS, Monatschr. f. Kinderh. **43**:289 (May) 1929.

The author reports three cases of megalacolon which in all respects resembled the Hirschsprung syndrome. These infants showed in addition signs of myxedema. On treatment with thyroid extract plus physostigmine, they made surprising recoveries. As they responded so readily to thyroid extract, Schippers does not believe that they had true cases of congenital megalacolon. In clinical symptoms and roentgen observations, however, there was a striking similarity.

He then digresses to the subject of true congenital megacolon. Basing his arguments to some extent on the reasoning of Marfan, he suggests his own theory as to etiology. He believes that the primary cause is a disturbance of enervation of segments of the large intestine. This leads to local meteorism and constipation, with resulting compensatory hypertrophy. At the transition of the sigmoid into the rectum, either the occurrence of folds of mucosa or an abnormally long flexure facilitates the hypertrophy. The usual secondary changes then take place.

Schippers lays special emphasis on enemas, laxatives and physostigmine for maintaining the tonus of the intestine, and an activated plant charcoal for meteorism.

GERSTLEY, Chicago.

LIPOID CELL SPLENOHEPATOMEGALY (NIEMANN-PICK). J. SCHMITZ and F. THOENES, Monatschr. f. Kinderh. **43**:341 (May) 1929.

The authors report a case of splenohepatomegaly in an infant, aged 20 months, with observations at autopsy. The blood showed: hemoglobin, 62 per cent; red cells, 3,400,000, and white cells, 3,000; the differential count, 60 per cent small and 7 per cent large lymphocytes. The urine was dark and showed considerable urobilinogen. Following splenectomy, the child died of pneumonia.

The infrequency of these diseases of the liver makes the clinical differentiation between this and the Gaucher type difficult. The following is suggested: As a rule, the peripheral lymph nodes are larger in the Niemann type. This point should not be overemphasized, as children are prone to enlarged lymph nodes from other causes. Leukopenia is perhaps more marked in the Gaucher type. This again is no certain means of differentiation.

The authors express the belief that the only important differential methods are the examination of the nervous system and of the liver. In the Gaucher type, there is unquestionably involvement of the nervous system as shown by changed reflexes. In the Gaucher type the liver is not enlarged as greatly as the spleen, while in the Niemann type the enlargement of the liver is especially marked.

GERSTLEY, Chicago.

CLINICAL DISCUSSION AND THERAPY OF PYURIA. HANS ARON and HERBERT HIRSCH, Monatschr. f. Kinderh. **43**:385 (June) 1929.

The authors attempt to contrast the development of the knowledge of disturbances in the urinary tract with disturbances of nutrition. They point out many points of similarity. In urinary diseases, the first effort in study was along pathologic lines with terms such as cystitis or pyelocystitis. Then came the era of bacteriology, with a pyuria coli instead of a dyspepsia coli. The authors continue the analogy by expressing the belief that urinary disturbances should be considered from the point of view of disturbances of nutrition. They like the term pyuria best.

They distinguish three types of pyuria: (1) a septic form resembling meningitis, (2) a secondary form associated with parenteral infections and (3) a chronic type without fever in girls of school age.

The treatment is mainly dietetic. Urinary antiseptics are placed in the same category as mild mercurous chloride and discarded.

The best results are obtained by a carbohydrate diet in connection with large amounts of water. In older children cane sugar, in younger children cane sugar combined with nährzucker and in infants nährzucker solutions alone are recommended. The authors use from 20 to 25 Gm. per kilogram of body weight and from 10 to 15 Gm. in older children. The daily amount never exceeds 250 Gm. The carbohydrate is dissolved in water, malt, coffee, weak tea and mixed with fruit juices. The total amount of fluid varies from 1 to 1½ liters, depending on the age of the child. In severe cases (meningeal type), enemas of from 25 to 30 cc. are given hourly if swallowing is difficult.

In children past the nursling stage, this diet is continued for two days and then cereal and zwieback are added. The high carbohydrate, low protein and salt diet is continued for from four to five days. In infants, after they are fed from one to two days on carbohydrate, the diet is changed to buttermilk with 10 per cent nährzucker.

The authors find that this treatment gives satisfactory results in thirty-nine case.

GERSTLEY, Chicago.

JUVENILE NEPHROSIS. HANS KNAUER, Monatschr. f. Kinderh. **43**:445 (June) 1929.

In a general review of the subject, the author expresses the belief that nephrosis is in some way related to the hydrolabile constitution. He then discusses the

clinical symptoms, and in one respect his views differ from the usual ones. Intercurrent temperature is usually held to be due to intercurrent infections, but the author lays emphasis on Stolte's theory that the cause may be a disturbance in water balance, as in thirst fever.

The author believes that nephrosis is a constitutional disease rather than an infection of the kidney alone. The disturbance is due not to a heightened affinity of the tissues for water but to a diminished ability of the blood to take up this water. Other constitutional symptoms are lowered blood pressure and a diminution in the trypanocidal substance in the blood serum. The latter points to involvement of the liver.

Treatment consists of the high protein, low salt and fluid diet. Thyroid preparations are of great value, particularly iodothyrin in large doses of 1 Gm. or more.

GERSTLEY, Chicago.

THE TREATMENT OF JUVENILE DIABETES WITH SYNTHALIN. J. LANGER, Monatschr. f. Kinderh. **43**:457 (June) 1929.

The author reports the cases of six patients with juvenile diabetes treated with synthalin. The results were satisfactory, and insulin could be dispensed with for long periods.

GERSTLEY, Chicago.

MEGALOSYNDACTILITIS; REPORT OF A CASE. H. ABRAMOVIES, München. med. Wchnschr. **22**:921 (May 31) 1929.

Cases of megalosyndactilitis are rare. A large digit caused by the union of the phalanges and the covering of the bony part of two fingers by a skin-muscle membrane was present in this case. Good photographs and roentgenograms of the hand are given. The case is reported for purposes of statistics and reference, without comment as to cause.

SCHORER, Kansas City, Mo.

SPLENOMEGALY; A SYMPOSIUM. Verhandl. d. deutsch. path. Gesellsch. **23**:7, 1928.

W. Hueck, Leipzig, in discussing the anatomy of the spleen, in the first of twelve papers comprising the symposium, concluded that the blood courses through the spleen in a closed circuit at least in embryonic life. O. Lubarsch, Berlin, proposed the following grouping for splenic enlargements:

1. Splenomegaly in circulatory disorders.
   (*a*) Disorders in systemic circuit.
   (*b*) Disorders in portal circuit — thrombophlebitic splenomegaly.
2. Splenomegaly in blood diseases.
   (*a*) Leukemia.
   (*b*) Pernicious anemia.
   (*c*) Hemolytic jaundice.
   (*d*) Thrombopenic purpura.
   (*e*) Erythremia.
   (*f*) Splenogenous anemia.
3. Metabolic disturbances.
   (*a*) Sugar and fat.
   (*b*) Gaucher and Niemann-Pick.
4. Splenomegaly in combined circulatory and metabolic disturbances.
   (*a*) Cirrhosis of the liver.
   (*b*) Banti's disease.
5. Splenomegaly in infections and intoxications.
   (*a*) Acute.
   (*b*) Chronic as endocarditis lenta, tuberculosis, syphilis, malaria, kala-azar, etc.

6. Splenomegaly associated with tumors.
   (*a*) Primary.
   (*b*) Secondary.
7. Splenomegaly due to animal parasites.
   (*a*) Echinococcus.

B. Ugriumaw, Leningrad, summarized the observations in sixty cases of splenomegaly. Of forty-three recorded cases the spleen weight was as follows: in three cases, from 500 to 1,000 Gm.; in twenty-three cases, from 1,000 to 2,000 Gm., and in seventeen cases, over 2,000 Gm. The largest spleen weighed 6,500 Gm. Fifty-five specimens were obtained from males; the small number from females, apparently being due to the reticence of Mohammedan women to permit observation by a physician. Half of the specimens were obtained from the bodies of persons from 20 to 40 years of age. In fifteen cases the liver was of normal size; in fourteen it was small, and in thirty-one it was enlarged. The only lymph glands found enlarged were the mesenteric, periportal and retroperitoneal. Histologically, it was found impossible to differentiate Banti's disease from hemolytic jaundice. R. Rössle, Basel, discussed the condition of the spleen following hemorrhage; stressed the analogy between the edematous pulp in this condition and in such things as acute infections and maintained the presence of a splenic enzyme in both conditions. In the discussion following the presentation of the foregoing papers, additional interesting features were observed. Bürger saw splenomegaly occur four times in infections with Bang's bacillus in the Kieler clinic in 1927. Ingestion of contaminated milk was the cause of the illness in all instances and the serum of the patients agglutinated Bang's bacillus and the bacillus causing Malta fever in high dilutions. Bang's bacillus was cultured in the blood. The characteristic picture of splenic enlargement developed after many weeks of remitting fever and the splenic tumor receded very slowly after treatment. Weicksel, in studying the red blood cells and the function of the spleen in blood transfusion, produced an anemia in dogs and then transfused them. He concluded that the spleen acted as a reservoir for the red blood cells. To further prove this he took photographs of the spleen in two projections and found that immediately after the transfusion the splenic volume was reduced one-fourth, while in from one to two hours it enlarged to a size larger than before the transfusion. Helly maintained that the normal vascular system of the spleen was closed but thought tears in the delicate splenic capillaries might aid in producing extravasations. Because of the delicate construction of the spleen, he also thinks injection methods are likely to produce erroneous pictures. Schilling stressed the three tissue components of the spleen, namely, the myeloid, lymphatic and reticulo-endothelial; he spoke of the spleen as a sponge the meshes of which might become engorged with any one of the aforementioned tissues, and advocated specifying which elements were involved in every type of splenic enlargement. Hamperl illustrated with a case report the impossibility of distinguishing the two types of lipoid cell splenohepatomegaly, Gaucher's disease and Niemann-Pick's disease. A child, 5½ months old, clinically had a lipemia and splenic puncture brought out cells from 30 to 60 microns in diameter, round or oval with one or more peripheral nuclei and a homogeneous protoplasm staining blue with Mallory's connective tissue stain. In addition, these cells were found post mortem in the liver, spleen, lymph glands, bone-marrow, lymphoreticulum of the tonsils and thymus and in the mucosal stroma of the small bowel near the Peyer's patches. The distribution of these cells was in accordance with the Niemann-Pick type. Furthermore, chemical analyses of the organs seemed to bear this out as the total lipoids were 9.6 per cent, total cholesterol 0.93 per cent and phosphorus 5.98 per cent. To confuse the issue, however, large quantities of Gaucher substance were found. Abrikosoff cited instances of chronic splenomegaly in which fungi of the aspergillus type were encountered morphologically and culturally. Sternberg doubted the occurrence of the fungi. He had seen encrustations of iron phosphate in a markedly atrophic spleen and noted the resemblance of these encrusted cords to fungi.

GEORGE RUKSTINAT.

THE ETIOLOGY OF MALACOPLAKIA OF THE BLADDER. Z. KAIRIS, Virchows Arch. f. path. Anat. **266**:788, 1928.

A case of malacoplakia of the urinary bladder is described in a girl, aged 1½ years, with an infected double kidney on one side. This disease is usually found in older persons. Cystoscopic examination shows the mucous membrane studded with yellow-white, raised plaques, with a depression in the center, and sometimes ulceration in the later stages. Histologically, the plaques are made up of lymphocytes and large round or angular cells, with small round nuclei, corresponding to fibroblasts, which are characteristic for the condition. There may also be iron-containing inclusion bodies. The condition has been variously regarded as a granuloma, the result of nonspecific infection, or of long standing cystitis. The latter seemed to be the causative factor in this case.

B. R. LOVETT.

COMPLETE RUPTURE OF THE RIGHT BRONCHUS. S. I. KRINITZKI, Virchows Arch. f. path. Anat. **266**:815, 1928.

A girl, aged 10 years, suffered a severe injury when a heavy wine cask fell on her chest. Twenty-one years later, at autopsy, a complete rupture of the right main bronchus 3 cm. below the bifurcation was found. The right lung was completely atelectatic, and, while the left showed marked tuberculosis, the right was entirely free from involvement.

B. R. LOVETT.

ANATOMY OF GAUCHER'S DISEASE IN INFANTS. H. HAMPERL, Virchows Arch. f. path. Anat. **271**:147, 1929.

In addition to the usual localizations (spleen, liver, lymph nodes and bone marrow), Gaucher cells were found in the cortex of thymus, tonsils, adenoids, lymph follicles of the intestine, zona reticularis of the suprarenal gland, and perhaps the lung. Kerasin and cerebrosin constituted 3 per cent of the dry substance of the spleen. The lipoids, phosphorus and total cholesterol were high, similar to the figures in Niemann-Pick's disease. The presence of Gaucher cells in the other organs is due to the special behavior of connective tissue and reticulum in the first year of life.

ALFRED PLAUT.

THE TREATMENT OF DIABETES WITH LOW FAT DIET. O. PORGES and W. ADLERSBERG, Wien. Arch. f. Inn. Med. **17**:1 (April) 1929.

The authors tried the effect of three types of diet—one almost carbohydrate-free with a preponderance of fat and protein; one low in carbohydrate and protein and high in fat, and a mixed diet with an abundance of carbohydrate.

They found that a low carbohydrate diet influenced the assimilation of sugar unfavorably, and that it definitely lowered permeability and favored the loss of sugar through the kidney.

A diet high in fat seemed to impair the assimilation of sugar. A diet low in carbohydrate seemed to impair the functional capacity of the insulin-secreting mechanism. The authors advance the theory that resting of this glandular function does not strengthen it, but seems rather to tend to greater insufficiency of its function. Adequate carbohydrate in the diabetic ration seems rather to make for increased sugar tolerance and decidedly enhances the effect of insulin.

The authors express the opinion that in diabetes one is possibly dealing with disturbances of innervation of the structures concerned with proper sugar metabolism. On the strength of this theory, they contend that stimulation through functional use and activity is indicated in the therapy for diabetes, rather than resting or functional disuse such as results from the customary diet high in fat and low in carbohydrate of the diabetic patient.

SCHLUTZ, Minneapolis.

PYLOROSPASM. WALTER BLOCK, Ztschr. f. Kinderh. **47**:281 (March 23) 1929.

In the feeding of patients with pylorospasm or stenosis, Block believes it important to give sufficient water even if the food is concentrated, and to give water retaining salts and carbohydrate, since these patients have a relatively increased need of nourishment and sometimes offer complicated feeding problems. In the worst cases, breast milk may not be the food of choice. If the x-ray pictures reveal a three hour limit for the emptying time of the stomach, this is not a sufficiently good indication of pylorospasm, since some stomachs empty slowly, and does not prevent a gain in weight, provided the vomiting is not excessive. Other cases are mild clinically but roentgenographically appear severe; this contradicts the opinion of Kerley that when pylorospasm is demonstrated by x-rays the use of atropine is without benefit. Some cases which seem mild in roentgenograms are really severe clinically and are confirmed as such at operation. The emptying time can be used in the diagnosis in doubtful cases, however; that is, a short emptying time contraindicates an operation. A 0.1 per cent solution of atropine, preferably in alcohol, given one and one-half hours before the feeding time, has helped considerably, as has atropine with phenobarbital (4 drops of a 0.1 per cent solution of atropine plus 0.015 Gm. of phenobarbital), four times during the day, or atropine plus intracutaneous injections of epinephrine hydrochloride, particularly when atropine alone has not been effective. But if there is a rapid loss of weight, which does not cease at the latest by the beginning of the second week, operation must be substituted for drugs. This is likewise the procedure for patients who after weeks of observation do not plainly improve, especially when they show more than the usual feebleness and great pallor in addition to a certain tense expression of the face. On account of the quick change for the better and the less care needed in nursing, Block now treats more and more patients by operation, in comparison with his former practice; in the last three years, nine of fifty-four patients with pylorospasm have been operated on. The after-care is important. Sufficient water to satisfy the water need should be given, of course, and not too much food because the metabolism, disturbed by lack of fluids and hunger, is easily upset and alimentary intoxication supervenes. Block gives from 15 to 20 Gm. of breast milk one and one-half hour after the operation, or buttermilk with from 3 to 5 per cent sugar at intervals of two hours; in the days following, he increases the amount to 100 cc. There may be temporary vomiting after the operation, but usually this is without significance.

EMERSON, Boston.

ANATOMY OF GOITER. L. ASCHOFF. Transactions of the International Conference on Goiter, Bern, Switzerland, Aug. 24-26, 1927. Edited by Hans Huber, Bern, 1928.

In order to understand the morphologic and etiologic genesis of goiter it is necessary to grasp the fact that the biologic curve of the goitrous thyroid is parallel to that of the nongoitrous thyroid gland. The curve of the goitrous thyroid is, however, more elevated than the other. From the morphologic point of view, goiter is a real hyperplasia of the thyroid.

In the curves of age incidence, there are several corresponding sharp rises to be noted, viz., the swelling or goiter of infancy, puberty and advanced age. In point of origin, they are to be distinguished as follows: (*a*) In the goiter of infancy, there is in addition to increased new formation a simultaneously increased moisture of the whole parenchyma. (*b*) The swelling or goiter of puberty is of chief importance, since on its degree essentially depends the intensity of the later developed adenoma. (*c*) In advanced age, a retrogression of the proliferating goiter of goiter may come to pass.

The biologic curve of the thyroid, goitrous or otherwise, is deformed by the development of the so-called adenomas. The germ of them occurs in all thyroids. In districts in which goiter seldom occurs they develop slowly and only to a certain size, in goitrous countries much faster and on occasion up to the size

of a child's head or even larger. This intensified development of the tumors, the so-called struma nodosa, depends especially on the enhanced metabolism of the goitrous thyroids.

In point of histologic origin, the adenomas present either an unphysiologic growth with immature (parenchymatous goiter) or riper stages (colloid goiter). According to the type of involution to which these tumors generally tend, the names of fibrous, calcified, hemorrhagic, cystic goiter are given. The nodular goiter originates commonly at or after puberty.

The question of etiology must be considered with that of the source of the general increase in weight of the thyroid in goitrous regions. Comparative histology supports the view that here an exogenous factor encountered in the surroundings is at fault, which leads to enhanced physiologic growth. According to chemical analysis of goitrous and nongoitrous thyroids, it must be assumed that the thyroid as a whole is continually striving for certain iodine content. When the supply is deficient, the absorbent surface of the thyroid increases through further growth of the parenchyma. Conformably thereto the percentage of iodine content is similar in the goitrous thyroid. Experiment indicates that it is not simply iodine deficiency which comes into play, but disturbed equilibrium between iodine and other substances.

The question of the periodic swelling or increase in size of the thyroid (that of pregnancy, infancy, puberty, advanced age and their respective forms of goiter) is independent from that of the goitrous swelling. Here factors at once endogenous and physiologic — among them perhaps an insufficiency of iodine metabolism or disturbances of iodine equilibrium connected with growth — have to be reckoned with

A sharp distinction must be drawn between endemic goiter and the thyroid of exophthalmic goiter. In this case the causative factor is endogenous and, in contrast to the swelling mentioned, pathologic. Simultaneous diseases of the thymus, suprarenal glands and lymphatic system warrant the conclusion that this cause attacks the nervous system and not the thyroid. The thyroid in cases of exophthalmic goiter is characterized by a special hyperplasia in the interior of the individual follicles. Intermediate stages occur between the hyperplasia in exophthalmic goiter and the parenchymatous goiter.

In contrast to the thyroid of exophthalmic goiter which shows marked symptoms of hyperthyroidism, in the goitrous thyroid it shows rather the picture of hypothyroidism in all stages down to complete cretinism. Only in a few cases does goiter exhibit hyperthyroidism; such are usually late forms of the goiter of puberty or so-called toxic adenoma.

Provided no signs of cretinism occur, endemic goiter displays no secondary influence on other systems. Goitrous heart, implying that the heart muscle is damaged by thyroidal toxins or bacterial toxins, is, according to morphologic evidence, nonexistent.

AUTHOR'S SUMMARY.

PATHOLOGIC ANATOMY OF THE MALIGNANT GOITER AND OF THE THYROID GLAND OF CRETINS. C. WEGELIN. Transactions of the International Conference on Goiter, Bern, Switzerland, Aug. 24-27, 1927. Edited by Hans Huber, Bern, 1928.

The malignant tumors of the thyroid gland are far more frequent in countries in which the goiter is endemic than in goiter-free regions.

The epithelial forms of the malignant goiter may be designated as carcinoma from a biologic point of view. Their malignancy is chiefly evident by the formation of metastasis. Histologically these neoplasms are often not ordinary cancers, but more differentiated and typically formed tumors which also always appear in the form of nodules. The highest degree of differentiation is reached by the metastasizing adenoma, a lesser one by the Langhans' proliferating adenoma and the least degree by the simple carcinoma. There are transitions which unite all these forms. They metastasize only after invasion of the blood vessels, especially of the capsular veins. The age of the patient must be considered as another important factor.

The malignant epithelial neoplasm, as well as the sarcoma and hemangioendothelioma, often originates in the nodules of old adenomas.

The study of histogenesis thus shows a connection of the malignant tumors with the common endemic nodular goiter. Efficacious prophylaxis of the goiter will therefore be able to diminish the incidence of malignant goiter.

Endemic cretinism is to be found only in districts in which goiter is endemic and in which the endemic has reached a high degree.

The thyroid of the cretin contains, as a rule, adenomatous nodules which, however, vary greatly in size. Almost without exception, they are parenchymatous and contain little or no colloid.

The structure of the thyroid tissue proper between the nodules shows characteristic changes, the epithelial cells undergoing a more or less severe degeneration. The colloid of the acini is scanty, chiefly basophil and the connective tissue is increased, forming a marked sclerosis. These changes are found in the highest degree in the atrophic thyroid glands of dwarf cretins.

The degeneration of the epithelial tissue of the gland begins early in the cretin. His thyroid gland functions in an inferior way, although part of its functions may be taken over by the adenomas.

The whole organism of the cretins is influenced by a hypothyroidism of different degree. The changes in the other organs show considerable resemblance or conformity with the changes seen in congenital or acquired athyreosis.

Regarding the etiology of endemic cretinism, external injuries of the thyroid gland, as well as hereditary factors, must be taken into account. The nature of the external factors is not yet known. The assumption that cretinism is a recurrence to the type of the primitive human races is not proved.

AUTHOR'S SUMMARY.

A DISCUSSION OF THE QUESTION OF POLYDIPSIA. A. H. MOLOCHOV, Collected Papers, Psychiatric Clinic of the First Moscow State University **2**:282, 1927.

The literature dealing with the subject of polydipsia is discussed by the author in an attempt to differentiate a primary psychogenic or neurogenic polydipsia from diabetes insipidus. There seems to be a clearcut group of cases in which one is not able to demonstrate any disturbance of the water metabolism and in which there is a pathologic craving for water, with marked exaggeration of the normal feeling of thirst owing to special psychogenic or neurogenic factors.

The author quotes three cases in boys, aged 4, 16 and 17, respectively. In the first case, a boy, aged 3½, developed polydipsia following whooping cough. Nine months after the onset of the symptoms, the boy was consuming twenty-five glasses of water a day. This was accompanied by a marked personality change. The child became cranky, irritable, restless, disrespectful and hit other children. Various metabolic studies gave negative results. Neurologic examination gave negative results. Once the boy passed some intestinal parasites following the administration of male fern. There was marked improvement in his condition after he left the clinic, especially in his social adaptations, although he still consumed large quantities of water. The boy was followed for a year after he was discharged from the clinic. Analysis of the case leads the author to the conclusion that one is dealing with special habit formations following whooping cough, as drinking of water helped the boy's "whoops."

The second case is that of a boy who had always been rather dull and unintelligent. Two months before the onset of the present illness, he developed a habit of spitting a great deal, associated with touching his genitalia with his right hand at the same time. The symptoms progressed so rapidly that one month after the onset of polydipsia, he drank two pails of water a day. He was studied extensively in the medical and psychiatric clinics with negative results as far as the metabolism was concerned. The x-ray pictures of the skull and sella were normal. Following treatment in the clinic with phenobarbital and restriction of fluid intake, there was marked improvement. Nine months after discharge, the patient drank only seven

or eight glasses a day. In the third case, there was a definite history of epidemic encephalitis.

The author concludes his article by stating that polydipsia even in the most extreme degree is not necessarily a symptom of diabetes insipidus, and that psychogenic factors may be just as important in the etiology of this condition. Unfortunately, when polydipsia starts first as a symptom of some underlying emotional factors it sets up a vicious organic cycle and leads eventually to an increased thirst due to concentration of the blood.

KASANIN, Boston.

WHITE BLOOD CELL PICTURE IN CROUPOUS PNEUMONIA OF INFANTS AND CHILDREN. KIYOSHI SAKAI, J. Pediat. (Tokyo), March 20, 1929, no. 346, p. 491.

The author examined the white blood cells in forty-one cases of lobar pneumonia in infants and children during the course of the disease and found that on the third day of the illness, the count reaches a maximum of 62,300 per cubic millimeter; between the fourth and eighth days, the count varies between 20,000 and 40,000. The count falls suddenly with crisis, and in convalescence it may reach even below the normal value. In case of resolution by lysis, the count gradually falls to normal. When two or more lobes are involved, the count is high, as is also the case in pseudocrisis and in the presence of complications. In the presence of complicating empyema, the count shows a long drawn out leukocytosis of moderate degree. The count seems to maintain no definite relations either to the age of the patient or to the type of fever present.

The polymorphonuclear neutrophils show the greatest increase on the third day, the maximum being 86.4 per cent, and the absolute number, 53,827. In a typical case, the percentage falls rapidly with crisis, approaching the number of lymphocytes. In complications or in pneumonia migrans, the number increases again, reaching the normal level gradually with recovery. In fatal cases, the percentage is high.

The lymphocytes show a marked decrease, giving the minimal figure of 7.8 per cent on the fourth day of the disease. The eosinophils usually disappear on the first day, and gradually reappear as the disease progresses to recovery. The mononuclears show a great variation, but in typical cases increase in percentage after crisis. In fatal cases, there is a marked decrease.

The plasma cells and Türk's irritation forms seem to appear at once after the crisis, and in protracted cases due to complications their appearance is both late and gradual. The basophils appear during convalescence, although not invariably.

KATO, Los Angeles.

Nervous Diseases

BRAIN TUMORS IN CHILDHOOD: A CLINICOPATHOLOGICAL STUDY. FREDERICK H. LEAVITT, Am. J. M. Sc. **178**:229 (Aug.) 1929.

The author, in reviewing the 350 case records verifying tumors of the brain, describes 23 cases, 15 of cerebellar gliomas. Twelve of the 15 cerebellar gliomas were in girls, and in the 8 other cases different types of tumors were found, showing the frequency of cerebellar gliomas compared with other types of tumors of the brain. There was a more or less general symptomatology which was noted through the series of cases, with a history of rather rapid onset in which the child became suddenly ill with vomiting and headache, soon followed by drowsiness and signs of intracranial pressure as noted by the rapidly choked disk with retinal hemorrhages, disturbance of gait, enlargement of the head and MacEwan's "cracked-pot" sign for infantile cases, plus the localizing symptom of the growth which can be determined by careful neurologic examination.

The author describes types of new growths with illustrations. He reports two cases of cerebral tumors occurring in identical twins.

The ratio of juvenile to adult cases is 1 : 14 in the author's series. Their favorite location is the cerebellum. They occur in this situation in more than 60 per cent of the cases. The "fetal-rest" theory of the genesis of neoplastic growths is supported by the identical occurrence of cerebellar tumors in monozygotic twins as reported by the author.

A plea is made for earlier recognition of cerebral neoplasms in children with obscure symptoms in the head.

For the cure and alleviation of distressing symptoms in patients suffering from tumors of the brain of all types, surgical and electrotherapeutic measures are of the utmost importance.

HENSKE, Omaha.

PARTIAL PARALYSIS OF THE LOWER EXTREMITIES IN CHILDREN, ACCOMPANIED BY BACKWARD MENTAL DEVELOPMENT. CHARLES C. DENNIE, Am. J. Syph. **13**:157 (April) 1929.

The author has studied eight children who presented a certain type of flaccid paralysis. There was also mental retardation in each case. The onset of the paralysis was sudden in three of the cases, while in five it was insidious. The Wassermann reaction of the blood was positive in three and negative in five of these children. All of them regained their power of locomotion under antisyphilitic management alone.

Mentally, however, they have remained stationary. The author names this clinical group, "incomplete flaccid paralysis of the lower extremities, accompanied by backward mental development," the etiology being syphilitic.

McBRIDE, Sioux City, Iowa.

NEUROPATHOLOGIC CHANGES IN A CASE OF LEAD ENCEPHALOPATHY. RUTH TUTHILL, Bull. Buffalo Gen. Hosp. **8**:15 (June) 1929.

A child, aged 2½ years, with a history of eating paint from window sills, died of acute lead poisoning. Histologic examination of the brain showed glial arborization of the molecular area of the cerebellum and sclerosis of the Sommer sector of Ammon's horn. This is the first time that changes of this kind have been recorded in lead encephalitis.

SANFORD, Chicago.

ENCEPHALITIS PERIAXIALIS DIFFUSA OF SCHILDER. F. R. FORD and J. J. BUMSTEAD, Bull. Johns Hopkins Hosp. **44**:443 (June) 1929.

Ford and Bumstead give a brief description of the morbid anatomy and clinical characteristics of Schilder's periaxial encephalitis, followed by a report of two cases with anatomic observations. The first ran an acute course for six weeks and was terminated by death from increased intracranial pressure. The anatomic changes were somewhat typical in that the process was not continuous, and four discrete lesions were found.

The second case was typical in respect to morbid anatomy, but the clinical picture was unique. The child had two sudden falls followed by paralysis and in one case by loss of consciousness. Each time marked improvement followed promptly, and once this amounted to substantial, if transient, recovery. Such an apoplectic onset has not been described in Schilder's disease previously.

LYTTLE, New York.

UNUSUAL LOCATION OF SOLITARY TUBERCULOMA. MORRIS GLEICH and A. M. SALA, New York State J. Med. **29**:81 (Jan. 15) 1929.

An encapsulated, solitary tuberculoma, 4 by 3 by 2.5 cm., was found in the left cerebral hemisphere above the optic chiasm at autopsy on a colored girl, aged 3 years. Few ocular and no neurologic symptoms were shown until two weeks before death.

AIKMAN, Rochester, N. Y.

SOME LABORATORY FINDINGS IN EPILEPSY. HAROLD A. PATTERSON, New York State J. Med. **29**:138 (Feb. 1) 1929.

In about 20 per cent of patients with epilepsy, albumin and casts are found in the urine within the first two hours after the attack and may not disappear before the fourth day. The blood picture is variable. Moderate or high leukocytosis may be shown, or the patient may have a persistent leukopenia. The occurrence in considerable numbers of a degenerated form of white cell, infrequently found in normal blood, seems to be characteristic of the disease.

Nonprotein nitrogen, uric acid, creatinine and serum protein increase during convulsions. Such high values may be mistaken for those in uremia. The blood sugar is usually low. No deficiency has been found in the calcium content. The spinal fluid pressure was found at the upper borderline of normal and was greatly influenced by external mechanical factors. The cell count, and the globulin, chloride and urea contents were normal, and the sugar value low. Of 1,000 patients with epilepsy who were tested for protein sensitization, from 37 to 56.8 per cent were sensitive as compared with 8 per cent among nonepileptic controls. Syphilis was found in less than 5 per cent of the cases.

Observations at autopsy frequently show no gross abnormalities, but microcephaly, hemiatrophy, chronic internal hydrocephalus, focal cerebral softening and tumors of the brain are the defects frequently disclosed.

AIKMAN, Rochester, N. Y.

VALUE OF CHILD TRAINING IN PREVENTION OF MENTAL DISORDERS. NEWDIGATE M. OWENSBY, South M. J. **22**:629 (July) 1929.

A large percentage of people are insane as the direct result of improper training received during childhood. There is an even larger number of persons affected with so-called "nerves" due to the same cause, wrong beliefs, habits of thought, suppressions, or fears inculcated by parents, teachers, and associates during childhood, which ultimately prevent their adjustments to the realities of life.

Because illness is the most convincing and convenient excuse for failure to meet an unpleasant situation effectively, their unpleasant emotions are unconsciously concealed and often present themselves disguised as physical symptoms.

The author believes that fears, inhibitions and other emotional disturbances inculcated into children during their early years, may cause abnormal glandular changes. Dementia praecox cases are possibly examples of such a connection.

SCHULTZ, Minneapolis.

RELIABILITY OF INFANTILE MEMORIES. J. A. HADFIELD, Brit. J. M. Psychol. **8**:87, 1928.

Modern psychopathology generally accepts the importance of early childhood impressions as a predisposing cause of the psychoneurosis. This makes important the question concerning the amount of reliance that can be placed on the adult's retrospective account of early experiences. Objections to their reliability are: (1) It is impossible for any one to remember that far back; (2) it is inconceivable that a child could have the thoughts ascribed to him.

There is no priori reason why an adult cannot recall childhood experiences. There is no question that the very young child has a memory and recognizes such things as the mother's breast very early in life. If it has a memory, there is no reason why it cannot be reproduced. These memories are usually of two types.

There are many reported instances of a spontaneous recall of an infantile memory. An instance of a child, aged 8, recalling a fire when he was 8 months, with checks indicating the reliability of the details is given. Then there are memories obtained by free association during an analysis and these fall into three groups: (1) memories that can be objectively verified; (2) memories that are corroborated from similar conditions observed in childhood, and (3) experiences commonly emerging in analysis which can neither be proved nor corroborated.

As an example of the first type, a case is cited of a man with bronchial asthma who, under hypnosis, recalled an experience of his mother putting something under his nose which nearly suffocated him. The mother verified the experience as occurring during her treatment for whooping cough. In this case the patient did not know that the event had actually occurred, even after he had described it.

In the second group, there are the experiences corroborated by observing similar behavior in children. All the symptoms of the psychoneuroses can be duplicated in childhood behavior of normal children. The factors leading to such behavior, however, are mostly subjective and observation of the actual causes is not an easy matter.

Can an experience happening at or before birth be recalled, is a question frequently raised. A case is described which gave an accurate description of the events and feelings surrounding the patient's birth, though she claimed no knowledge of such things from personal observation. The story was reproduced with all the emotional vividness of a relived experience. Watching a child at birth and after leads one to realize that the feelings of terror and anxiety and of strangulation might be experienced, and an adult reviving such a memory might be actually recalling such feelings.

The third group do not lend themselves to either objective verification or corroboration but are the recall of subjective impressions of an early experience. As an example, a detailed account of an early childhood experience is given, in which a revulsion to the mother's breast is described and this was associated with the administration of an enema, and fondling by the father who was drunk. If such an account is taken as a recall of early impressions, then it is certain that the child's experiences are much richer and fuller than a superficial observation would suggest.

Except for the regularity of the reproduction of such experiences one would be inclined to dismiss them as the fabric of the imagination. There are two other possible considerations: (1) that they are literally true; (2) that a real experience has been interpreted and colored by later experiences. All experiences related during an analysis are not based on fact. Some are symbolic; some are composite; some are pure fantasy. The imagination and the fantasy are interesting and important. The reading into a past experience of the attitude of the present is also possible, and yet the present is colored and directed by the past and therefore bears an important relation to it.

The mind of a child consists mainly of feelings which are vague and not differentiated. When one accepts that feelings as well as thoughts can be reproduced and also accepts that the sophisticated language of the adult which is used to describe these infantile feelings is a mixture of words describing both feelings and interpretations of them, one clears up some of the difficulty about the reliability of infantile memories.

The mind of the child consists of vague and undifferentiated feelings, some of which are later shaped into thoughts. These feelings are not different in kind from those experienced in later life. But the adult groups his feelings and differentiates between them — the child has not the capacity to do this. Children are too young to understand, but never too young to feel. The fact that the feelings are not understood but strongly felt is one explanation why some experiences have such a profound effect on the mind of the child. These are the experiences which may be recalled even though the language in which they are recalled is the product of a much later period. Archaic memories might be explained, not as an inherited endowment but as "merely the later interpretations of crude and primitive feelings closely associated with organic needs" and sensations. The organic feeling may be the only archaic factor.

Feelings can be reproduced as well as thoughts, and they can be expressed either by the primitive emotional response itself or by language. The infant has only the former and the adult in an analytic situation may find that a situation can be reproduced only through feeling it. The language used to described it may be the true interpretation of this experience.

In translating the feeling into words there are three possibilities: (1) pure translation; (2) interpretation in the light of later experience but retaining the correct explanation of this feeling, and (3) interpretation so colored by later experience that the original feeling is invested with a wrong meaning. It is on this question of interpretation that large differences of opinion exist. The example is given of the boy who slashes off the heads of flowers, and it is then discovered that the flower represents the father. Adler and his followers would interpret this as a striving for power and the elimination of the father who thwarts this craving. Freud and his followers would place a sexual significance on this eliminating of the father as a means of satisfying desires with the mother. The previous formulation and school of thought would cause the analyst to read his own interpretation into the facts. This type of fallacy can come from both analyst and patient; from the analyst by reading in his own interpretation and from the patient ascribing to early experiences the interpretations of a later period.

The present view of freudians is to regard as of little significance the question about the reality or unreality of the experience. It is the wish for incest or the fear of castration that form the important things, and they exist apart from real experiences. Freud is quoted as saying "I should be glad to know whether the primal scene was a phantasy or a real experience. But taking similar cases into consideration, I must admit that the answer to the question is a matter of little importance." Since the whole freudian psychopathology is based on recollection, it leads one to ask what is left of the whole system when it is of little importance whether or not these rather objective experiences are true or not.

Besides objective verification of a recalled childhood memory, there are other things that should lead one to take these memories seriously. The warmth and feeling with which an experience is recalled is different from that associated with an imaginary experience. Another factor is strong emotional tone and the effect such recall has either in producing or in abolishing symptoms. The witnessing of such recollections strongly impresses one with the reality of the experience. The final factor that is convincing is the fact that the psychoneuroses and the character traits are so fully explained by the memories brought out by free association.

All of these considerations are not to be considered as positive proofs. It is only the cumulative evidence which commands that the fact be taken seriously when associated with the factors enumerated. Absolute proof for the capacity to recall infantile memories is not possible. Evidence points to the possibility of such recall. Skepticism may be justified but "complete incredulity can only be a mark of prejudice."

ALLEN, Philadelphia.

NOTES ON A PEDIGREE OF AMAUROTIC FAMILY IDIOCY (TAY-SACHS' DISEASE). D. D. STENHOUSE STEWART, Brit. M. J. **1**:101 (Jan. 19) 1929.

The author comments on the rarity of references to this condition during the past twenty-eight years as compared to their plentiful appearance in the first twenty years succeeding its first description by Waren Tay in 1881. He then reports a case of this disease occurring in the second generation of the classic R. family, which was recorded by Kingdon, of Nottingham, in volume 80 of the "Transactions of the Medico-Chirurgical Society." Of twelve children, six died of this complaint, and in two, extensive postmortem examinations were made by Risien Russell. Of the remaining six, the eldest daughter is unmarried. In the family of the elder son, there is one living child, one pregnancy terminated in a "mole," and another child died of meningitis. The patient whose case is reported was the second child of the next daughter, and died in convulsions. A boy born to the same mother is now 7 years of age and well. One other sibling has a healthy daughter aged 2½ years. The author raises the question whether or not the succession is solely through the distaff line. He asks whether matrimony should be advised against and also for suggestions as to the prenatal and postnatal treatment in any further pregnancies.

A. KNAPP.

JUVENILE BEHAVIOR DISORDERS IN EPIDEMIC ENCEPHALITIS: THEIR TREATMENT BY BULBOCAPNINE. T. R. HILL, Lancet **1**:968 (May 11) 1929.

The behavior disorders that are commonly observed in children following an attack of epidemic encephalitis are: pursuit of the child's own way, impulsiveness, lack of self-control, lack of concentration, disobedience and defiance. In their most severe form, they are seen in children who are free from parkinsonism or who suffer only from hemiparkinsonism.

As the behavior disorders are due to organic disease, attempts at psychotherapy are illogical and have proved futile. All of the common narcotic and hypnotic drugs proved ineffectual except in such large doses as to induce sleep.

Encouraging results have been obtained by Gadamer by the employment of bulbocapnine, an alkaloid extracted from *Corydalis cava* (bulbe creux). When given in doses of from 0.1 to 0.2 Gm. three times a day, whether by mouth or hypodermically, it exerted a marked beneficial action on the mental state and behavior. This action continued only as long as the drug was given. The longest period that the drug was given was eight weeks. Absorption and elimination of the drug were rapid. At first after the administration of the drug, there was a period of drowsiness lasting from ten to thirty minutes; then the patients were normally awake with marked diminution of the abnormalities of mental state and behavior. This effect lasted for several hours after the dose.

LANGMANN, New York.

PORENCEPHALY WITH MYOCLONUS AND CONGENITAL HEART LESION. J. M. ALLEN and C. WORSTER-DROUGHT, Proc. Roy. Soc. Med. **22**:392 (Feb.) 1929.

A boy, aged 4 years, was taken to the hospital because he was unable to walk or talk properly or to feed himself. He was not clean in his habits and was constipated. He tried to crawl at 3½ years of age. He could move both arms freely, but with apparent aimlessness. He held them in a position of flexion when at rest. There was a soft systolic murmur replacing the first sound of the heart; this was heard best over the third left intercostal space. The cerebrospinal fluid was normal. The Wassermann reaction was negative.

WILLIAMSON, New Orleans.

MONGOLISM WITH ENLARGED LIVER AND JAUNDICE. RONALD CARTER, Proc. Roy. Soc. Med. **22**:392 (Feb.) 1929.

The patient, aged 2 years, was taken to the hospital on account of jaundice. The general aspect of the child was that of a mongol. There was marked jaundice with an enlarged liver which was 3 fingerbreadths below the costal margin. The stools were normal in color, and there was no bile in the urine. The jaundice disappeared completely within two weeks, but the liver remained large. The Wassermann reaction was negative and the family history unimportant.

WILLIAMSON, New Orleans.

DIABETES IN A MONGOLIAN IMBECILE. DOROTHY C. HARE, Proc. Roy. Soc. Med. **22**:1031 (June) 1929.

The patient was 7 years of age. At the age of 6 years she had suffered from an attack of measles, after which the symptoms of diabetes had been noted. The blood sugar was 0.4 Gm. per cubic centimeter. She improved rapidly on treatment with insulin. Her development showed typical mongolian characteristics, and her mentality was of a low grade. The author felt that the incidence of diabetes in mongols is rare, as she could not find any case reported in the literature.

WILLIAMSON, New Orleans.

OCULAR TROUBLES IN CERTAIN CASES OF TUMORS OF THE ANTERIOR FLOOR OF THE CRANIUM; MENINGIOMAS OF THE CRIBRIFORM PLATE. M. J. CHAILLOUS, Ann. d'ocul. **165**:881 (Dec.) 1928.

Meningiomas or endotheliomas of the dura are tumors seen along the entire cerebrospinal axis, and occur so frequently in the brain that Cushing said that

of 1,398 intracranial tumors, 12 per cent were of this type. These tumors begin slowly and frequently attain astounding proportions before either subjective or objective symptoms appear. At times they are invaded by osseous projections, which make the complete removal of the mass difficult. However, to prevent a recurrence, it is necessary to remove entirely the invaded tissue. Frequently, recurrences take place. In one case quoted from Cushing's series there were eleven, and in another five, recurrences. In his atlas dated 1835, Cruveillier gave an excellent illustration of a meningioma of the cribriform plate of the ethmoid. In 1911, Cushing examined a patient post mortem, who had complained of blindness and mental disturbance. Again in 1921, he saw a similar case. Both of these patients had succumbed after a decompression.

Kennedy, in 1911, was the first to draw attention to a syndrome observed in lesions localized in the anterior part of the cranium. It was characterized by the unilateral loss of smell and vision, with primary optic atrophy of the same side and papillary edema of the opposite side due to intracranial compression. There was also a mental disturbance. Two other cases were reported by Siewers in 1921, with similar symptoms in addition to a large central scotoma in one case.

A patient operated on in 1922 by Cushing had a meningioma weighing 60 Gm. which was removed in three sessions. The preoperative diagnoses in this instance had been aneurysm of the internal carotid, ethmoiditis, frontal tumor and pituitary tumor. An intranasal operation had been performed, and roentgen irradiation to the pituitary region had been given.

The author reports the history of a patient, operated on by de Martel, in whom 80 Gm. of a tumor was removed from the anterior portion of the cranium. On account of a profuse hemorrhage, it was impossible to complete the operation.

He groups the cases under two types: (1) those showing atrophy of one optic nerve and edema of the other; (2) those showing a retrobulbar neuritis, in which the diminution of vision is not accompanied by any objective sign for a certain length of time, and then a primary optic atrophy develops. The first type is not so difficult to diagnose. The second, however, may be mistaken for toxic and infectious retrobulbar neuritis as well as for that due to multiple sclerosis.

In summarizing, the author says that one should think of meningioma if the following signs are present: (1) diminution of vision; (2) retrobulbar neuritis; (3) unilateral optic atrophy, with beginning edema of the other disk; (4) central scotoma; (5) exophthalmos on the side of the lowered vision, and (6) mental disturbance.

H. W. SCARLETT.

THE REFRACTIVE INDEX OF THE CEREBROSPINAL FLUID IN NORMAL AND PATHOLOGIC CONDITIONS. A. SIGNA, Pediatria **37**:747 (July 15) 1929.

The author studied the refractive index in cases of tuberculous meningitis, purulent meningitis, acute epidemic encephalitis, diseases not directly affecting the nervous system and in normal cases.

He concludes that the refractive index varies within wide limits in both normal and abnormal cases.

The extreme values found in various diseases are not such as to allow the determination of the etiologic factor.

The average values nearest to the normal are obtained in epidemic encephalitis.

Fluids with a refractive index above 1.33532 may be considered of inflammatory origin.

SALA, New York.

CEREBRAL ABSCESS; REPORT OF A CASE. M. ACUNA and P. WINOCUR, Arch. latino-am. de pediat. **22**:287 (May) 1929.

The case concerns a child, aged 10 years, who had had a recurring double otitis media since the sixth year.

In the final attack, meningeal symptoms supervened. The spinal fluid revealed the presence of a purulent meningitis of the pneumococcic type.

SCHLUTZ, Minneapolis.

CONGENITAL AND HEREDOSYPHILITIC ENCEPHALOPATHIES. F. BAZAN, C. A. CORREAS and J. C. DERQUI, Arch. latino-am. de pediat. **22**:312 (May) 1929.

The report is based on twenty-five well controlled observations.

The authors believe that the rôle of syphilis as a causative factor in the development of encephalopathies, while large and predominant, has been exaggerated by many observers.

In only three of their cases was syphilis actually present. In three others, its presence was doubtful. In the nineteen remaining cases, it could definitely be excluded.

SCHLUTZ, Minneapolis.

A FORM OF PROGRESSIVE MUSCULAR DYSTROPHY NOT DESCRIBED IN THE LITERATURE. J. M. VILLACIAN, Rev. españ. de med. y cirug., December, 1928.

Two cases are reported of primary myopathy of hereditary character in a brother and sister. The hereditary character of the disease is shown in the fact that the father, an uncle and an aunt of the patients died of the disease, which developed also in two sisters, one brother and in one cousin. The disease begins between the fortieth and forty-fifth year, is of progressive character and ends fatally from ten to fifteen years after the onset of the symptoms. The latter are: localization of the atrophic segments in the proximal parts of the limbs; symmetrical character of the atrophy and similarity of posture and gait while standing, walking, climbing, descending and getting up in the two patients studied; exaggeration of the lumbar flexure and displacement of the scapulas; lack of idiomuscular contraction; abolition of tendon reflexes and of electrical reactions. Motor weakness and atrophy begin almost at the same time in the arms and legs. The muscles of the head, neck and tongue are not involved. At first there are painful cramps, and afterward a sensation of stiffness during sudden flexion of the limbs.

The male patient was found to be suffering from syphilis (positive Wassermann reaction of the blood and other clinical symptoms). His sister probably suffered from the same disease, judging from certain symptoms observed, but serologic tests were not carried out. The author does not express definite opinions on the causal relationship of syphilis and the muscular dystrophy in the cases studied. No symptoms of endocrine disturbances were noticed, and opotherapic treatment failed to produce beneficial results.

NONIDEZ, New York.

FLATTEAU'S SIGN IN INFANTILE MENINGITIS. E. FILGUEIRAS, Arch. de pediat., Rio de Janeiro **8**:267 (May) 1929.

In three cases of meningitis in infants under 1 year of age, the author found that Flatteau's sign (nucopupillar) appeared at about the same time as rigidity of the neck. As Kernig's and Brudzinski's signs are not always easily obtained in young infants, this sign should be of value.

SANFORD, Chicago.

TREATMENT OF CHOREA WITH PHENYLETHYLHYDANTOIN. ADELBERT GOTTLIEB, Monatschr. f. Kinderh. **43**:433 (June) 1929.

The writer recommends phenylethylhydantoin as superior to phenobarbital in the treatment of patients with chorea. In seventeen patients treated during the last two years, he finds that the duration of the disease was reduced to three weeks, where it had formerly been six weeks.

GERSTLEY, Chicago.

RESULTS OF PHENYLETHYLHYDANTOIN THERAPY. WALTER LENGSFELD, Monatschr. f. Kinderh. **43**:469 (June) 1929.

The writer reports results in thirty-five cases of chorea. He reviews the literature to some extent and finds that a number of authors have reported toxic symptoms in the bone-marrow, kidney and intestine. He therefore uses the drug carefully, giving 0.075 Gm. three times a day and increasing the dose gradually to 0.15 Gm. three times a day. He believes that the use of phenylethylhydantoin

constitutes the best method of treatment for chorea. It does not prevent recurrence nor does it alter the child's resistance to rheumatic infection.

GERSTLEY, Chicago.

THE TREATMENT FOR HYDROCEPHALUS. L. SCHÖNBAUER and K. HUTTER, Wien. klin. Wchnschr. **42**:806 (June 13) 1929.

A boy, aged 11 years, with hydrocephalus, received twelve roentgen treatments of the choroid plexus, with no benefit. In order to conserve what power of vision remained, the choroid plexus of the left side was exposed and subjected at several points to electrocoagulation. No hemorrhage resulted. For a period of one and one half years, clinical improvement was observed; then decompression relieved the failing vision.

CLAUSEN, Rochester, N. Y.

CONJUGATE OCULAR MUSCLE SPASM IN CHRONIC EPIDEMIC ENCEPHALITIS. H. SJÖGREN, Acta ophth. **6**:97, 1928.

Sjögren reviews the references to ocular disturbances accompanying chronic epidemic encephalitis gathered in the literature and the cases which he studied in the Serafimerlazarette Clinic. He notes that paroxysmal tonic attack of conjugate deviation of both eyes upward and outward seems most prevalent. Occasionally the deviation is downward but rarely in other directions. The onset is sudden and involuntary. As a rule, the patient displays some fatigue or exhaustion before the muscular spasm manifests itself. A psychic stimulation may bring on the muscular disturbance. When the eyes are in the abnormal position, they remain fixed for a considerable period and the position cannot ordinarily be altered at will. Frequently, a nystagmus in various directions has been noted. The palpebral fissures are widely separated, and the lids cannot be closed voluntarily. Occasionally, a clonic blepharospasm has been observed. The patient as a rule is conscious of the disturbance, which may last from a few minutes to a whole day. The spasm is often painful and uncomfortable. Often the patient presents other parkinsonian symptoms, especially a facial weakness.

Sjögren reviews the various theories proposed by previous writers. He is not in accord with their assumptions, but believes that the process resembles that disturbance in the seventh nerve which was described by Bell in 1811.

A. M. YUDKIN.

THE EFFECT OF INFECTIONS ON THE VEGETATIVE NERVOUS SYSTEM OF CHILDREN. ALOJZ CHURA, Čas. lék. česk. **65**:1035 (July 2) 1926.

The author reviews the work of E. F. Muller on the increase and decrease of peripheral white blood cells after various reactions. He concludes that the peripheral leukopenia after such reactions as freezing is due to vasodilatation of the mesenteric vessels and to accumulation in the liver. The reaction is brought about through both the sympathetic and the parasympathetic portions of the vegetative nervous mechanism. In peripheral leukocytosis, a vasoconstriction of the mesenteric vessels takes place. Such diseases as measles are valuable for watching the effect on the vegetative system, the parasympathetic system during the onset and the sympathetic after eruption of the rash. Calcium seems to have some effect in keeping the influence of the parasympathetic system in the ascendant.

STULIK, Chicago.

EPILEPSY AND ALLIED CONDITIONS IN CHILDREN. WLADYSLAW STERLING, Pediatria Polska **9**:1 (Jan. and Feb.) 1929.

The author reviews much of the literature and concludes that a great amount of work has been done along this line but that the cause and the pathology of epilepsy and allied conditions are yet unknown. He claims that the age at which epilepsy usually occurs is between 6 and 7 and between 12 and 15 years. There

is a great difference in symptomatology between the epilepsy of the child and that of the adult because in children the nervous system is not completely developed. There are cases on record in which a patient with true epilepsy recovered without any treatment.

The allied conditions that the author speaks about are: psychic fits occurring in mentally deficient children, polyclonia epileptoides continua, affect epilepsy in which Chvostek's sign is present, hemitonia paroxysmalis, spasmophilia, breath-holding, vasovasal attacks, hysteria, jacksonian attacks, tetanica parathyropriva, epilepsia extrapyramidalis, convulsions due to worms, Ménièr's disease, pyknolepsy and narcolepsy.

KRUPINSKI, Chicago.

THE PROGNOSIS OF HEINE-MEDIN'S DISEASE IN THE LIGHT OF OBSERVATIONS AT AUTOPSY. YOSHITAKA NAKANO, J. Pediat. (Tokyo), March 20, 1929, no. 346, p. 471.

The author had occasion to examine the necropsy material extensively in a case of anterior poliomyelitis in a child, aged 5 years, who made an uneventful recovery from the acute attack of the disease, but who suddenly died during the convalescent period. The death was sudden and was not accompanied by any signs of acute illness, taking place on the fortieth day after the first signs of the acute attack. On microscopic examination of the central nervous system, the author found a moderately severe involvement of the medulla, although during life there were no symptoms referable to the bulbar condition. He is of the opinion that in the so-called purely spinal type of poliomyelitis the medulla may also be affected, and that this may be the cause of sudden death during convalescence. Again, the author found an ample evidence of lymphatism in this case, as there was a true hyperplasia of the thymus gland together with a generalized lymphatic enlargement throughout the body.

KATO, Los Angeles.

Diseases of the Eye

PERSISTENT PUPILLARY MEMBRANE AND CONGENITAL ECTOPIA LENTIS. A. R. CREBBIN, Am. J. Ophth. **12**:87 (Feb.) 1929.

A boy, aged 11, is said to have been born with a "misshapened pupil." One brother has 4.50 degrees of hypertropia, and a cousin is blind from congenital retinal pigmentary degeneration. The right eye is slightly exotropic, and the pupil eccentric up and in. The left pupil is eccentric upward but less so than the right. Both irides are tremulous, and both anterior chambers irregularly deep. Across both corneas, above, is an opaque advance of the limbus. The right lens is luxated in and slightly down; the left, up and in. Each eye shows a cobweb-like membrane arising from the lesser circle of the iris, and containing an irregular hole corresponding to the undilated pupil. This membrane is more marked in the right eye. Some suspensory ligament fibers can be seen in the aphakic portion of the pupil.

W. S. REESE.

OPHTHALMIC SCHOOL CLINICS. T. HARRISON BUTLER, Pub. Health Rep. **42**: 251, 1929.

From sixteen years' experience with school clinics, Butler feels that attention to the eyes of young children is of outstanding importance. Children with ametropia or imbalance of the ocular muscles may suffer from asthenopia, which interferes with their education; and, worse still, through defective monocular or binocular vision, they may acquire an inferiority complex which they are apt to carry through life.

Butler is convinced that the work of an ophthalmic school clinic should be done by an expert ophthalmologist, one who has a sound knowledge of general medicine and of the special diseases of children, and never by an amateur. Only in this way can the interest of the child's visual mechanism be best served.

Butler's school clinic is attended by all school children in Coventry who fail to attain 6/9 acuity with either eye. These preliminary tests are carried out by nurses and teachers in the school, standard conditions of test type and illumination being utilized. Shyness of the little patients is overcome by congregating parents and children in a common clinic and by having the children observe the examination of their schoolmates. The examination in each case consists of manifest refraction without and with glasses that the children may possess, of induction of cycloplegia with three instillations of 1 per cent solution of atropine in each eye at half hour intervals, of careful retinoscopy with a flat mirror in a dim but not dark room, of verification of the retinoscopic examination in the trial case, and finally of examination of the eyes by focal light and of the fundi by the ophthalmoscope.

For the adequate correction of refractive errors of children, Butler emphasizes the need for accurate retinoscopy. The common sources of error in retinoscopy that he points out are:

1. *Incomplete Cycloplegia.*—Whenever 3 drops of 1 per cent solution of atropine fails to give the desired result, a prescription for drops at home is given.

2. *Estimate of Retinoscopy Not Made at Macula.*—An estimate of retinoscopy not made at the macula is a common fault and one that may yield several diopters of error. The remedy is to have the child look at the retinoscope mirror and to check the accuracy of his fixation by observing the position of the image on the cornea.

A prescription for glasses is given after the retinoscopic observations are verified at the trial case. No deductions are made for myopia. In hyperopia, if the error exceeds 8 diopters, 2 diopters are subtracted for cycloplegia; if the error is less than 8 diopters, then 1 diopter is subtracted for cycloplegia. In astigmatism, if the cylinder exceeds 4 diopters, from ½ to 1 diopter is subtracted, while no subtraction is made for cylinders of less than 4 diopters. After the lapse of a month, all children to whom glasses are given are reexamined to check up the fit of the frame, the accuracy of the lens and the visual acuity.

Butler looks on concomitant strabismus as a disorder in which the underlying cause is congenital weakness of fusion, and in which the precipitating cause is anisometropia. He does not have much faith in fusion training with the amblyoscope, stereoscope and other devices. To overcome difficulties in fusion, he feels that the best aid is to equalize the visual acuity for each eye through complete occlusion of the fixing eye, "so that no light can enter." Atropine in the fixing eye does not suffice. In his experience, the occluded eye does not suffer in acuity. In this way, he feels that 70 per cent of the amblyopic eyes in children under 8 years of age can be brought to full normal acuity at the rate of one Snellen line a month. Failure to restore acuity to an amblyopic eye may be encountered chiefly in boys, but principally in any child who has passed the age of 10 years.

If strabismus persists, after the utmost has been done to revive the acuity of the squinting eye and after proper glasses have been worn for at least a year, then Butler proceeds with operation. He does not recommend free tenotomy, but always an advancement of the appropriate muscle combined with a recession of its antagonist.

Butler looks on myopia as a hereditary tendency and one likely to progress after debilitating disease. He notes that myopia is more prevalent in mining and agricultural communities where close intermarriage is the rule than it is in cities where the opposite is true. He points out that the introduction of games into the schools of Sweden brought about a decrease in the amount of myopia in Swedish school children. His practice is to allow a myopic child to continue in school in the normal manner, but to insist that outdoor games supplant music lessons, light reading and other confining interests. He cautions against haste in returning to school of a child who has passed through a debilitating illness, until the child has had the benefit of a long convalescence in the open air with plenty of wholesome food.

J. H. WAITE.

FUNCTIONAL DIPLOPIA IN A SCHOOL BOY. A. M. MACGILLIVRAY, Brit. J. Ophth. **12**:588 (Nov.) 1928.

A healthy, highly intelligent boy, aged 8 years, had periodic attacks of double vision for six months. In reading, the patient saw two words instead of one, each word standing clearly alongside of the other without overlapping. When reading from test charts he read each letter twice, with either eye separately or with both eyes. The vision in the right eye was 6/6 and in the left eye, 6/12. In all other respects, the eyes functioned normally and revealed no abnormality. The refraction was a low grade hyperopic astigmatism. Malingering was eliminated. No treatment was given. The child was assured that the trouble would disappear, and it was advised that no allusion be made to the double vision in his presence. Double vision had disappeared on examination six weeks later and had not recurred one year later. The vision was then 6/5. The author considers the condition purely functional.

W. ZENTMAYER.

CATERPILLAR HAIR OPHTHALMITIS (OPHTHALMIA NODOSA). R. FOSTER MOORE, Brit. J. Ophth. **13**:57 (Feb.) 1929.

A case is reported in a boy, aged 12. Fourteen days previously, the right eye had been struck by a thrown caterpillar, said to have been a "woolly bear." There was a general diffuse injection of all the ocular vessels; there was no staining of the cornea. The anterior chamber was half full of pus, and numerous fine deposits were present on the back of the cornea. The pupil dilated fully. Intolerance of light was a marked feature. The sight was greatly impaired. Three fine hairs were to be seen deeply embedded in the cornea. Attempts at removal failed. No hairs were to be seen in the conjunctiva, and no nodules were present at any time in the course of the disease. At the end of five weeks, the symptoms had largely abated. A considerable exudate in the vitreous had been mostly absorbed. The biomicroscope revealed several additional hairs extending deeply into the substantia propria. Three and a half months after the injury, the eye was quiet. The hairs could be seen apparently at their original site. Vision was 6/6. The exceptional features in the case were the early appearance of severe symptoms; the steady improvement, without exacerbations of the symptoms after obvious improvement set in; the absence of nodules in the conjunctiva episcleralis, and the complete recovery. It is pointed out that the barbs of the hair of the "woolly bear" caterpillar are directed forward toward the point of the hair and would therefore seem to be planned to prevent their penetration. While the suggestion that the hairs contain some form of poison appears to lack confirmation, it would seem that the severity of the inflammation with the formation of hypopyon, and its long course, would strongly suggest that it was not due simply to the presence of a small, inert, foreign substance in the cornea, but that some potent poison was responsible for it.

W. ZENTMAYER.

DOES "SCHOOL MYOPIA" EXIST? H. BIRBAUM, Arch. d'opht. **46**:38 (Jan.) 1929.

The author believes that the evolution of refraction from the hyperopia present at birth corresponds to the elongation of the eye with growth. Much work has been done to explain how school work produces myopia without showing that this is the only cause. It cannot be proved that these children would not have been myopic without school work.

If it is true that myopia increases while at school it is also true that hyperopia diminishes. Consequently, those eyes that are less hyperopic at birth have a greater chance of becoming myopic. On this ground an increase of from 1 to 2 diopters of myopia is no more a pathologic condition than a decrease of hyperopia from 4 to 2 diopters. The fact that myopia increases more than hyperopia decreases is a purely mathematical problem. A long eye which lengthens 40 per cent will be much longer proportionately than a short eye which elongates 40 per cent. The

author reviews the evidence in favor of the ontogenetic evolution of myopia and refraction in general. In closing, he quotes Landolt, who suggested that the tendency to myopia can be looked on as a phenomenon of adaptation in the struggle for existence.

S. B. MARLOW.

DOES SCHOOL OR OCCUPATIONAL MYOPIA DEPEND ON CLOSE WORK, OR IS SOME OTHER FACTOR RESPONSIBLE FOR IT? OSKER HEINONEN, Acta ophth. **6**:238, 1928.

From his observations of the refractive errors in school children from different social strata, Heinonen noted the presence of a slightly higher percentage of myopia among the children of intellectual workers, and that persons with myopia who do not belong to the intellectual group but attain higher education are more myopic than their parents. The peasant teacher who is myopic often has a greater myopic error than his progenitor. The percentage and severity of myopia seems to increase in the higher grades of school life. The author's statistics show that near work in school is not the dominating factor in producing myopia. He believes that the intellectual endowment of the person is intimately bound up with myopia. This probably accounts for the greater percentage of myopia in the children of school teachers than in those of other classes.

A. M. YUDKIN.

Diseases of the Ear, Nose and Throat

THE LEUKOCYTIC RESPONSE TO THROAT INFECTIONS. JOHN H. MUSSER, M. Clin. N. Amer. **12**:1377 (March) 1929.

Infection in the throat may provoke four changes from the normal in the leukocytic picture: an increase in polymorphonuclears; an increase in mononuclears; leukopenia with diminished or absent granulocytes, and leukocytosis with relative hypogranulocytosis. The first type of response is seen in such infections as quinsy and in streptococcal sore throat, and the biologically closely related scarlet fever. In these conditions, a hyperleukocytosis with polymorphonuclear increase is usually found. The second variety occurs in infectious mononucleosis, in which there is a slight but absolute reduction in the granular cells and a relative and absolute increase in the mononuclears. The latter cells are of three types: normal small lymphocytes, large mononuclears and a mononuclear cell not usually met with in normal blood. This leukocytic response is a specific one, not due to a peculiar reaction of the individual. The third reaction occurs most typically in agranulocytic angina, a syndrome characterized by necrotic inflammation of the tonsils, gums and mucous membrane of the mouth, jaundice and the absence of granulocytic cells in the peripheral blood. Vincent's angina probably belongs to this category. The same type of reaction occurs in other nonrelated conditions such as aplastic anemia, benzene poisoning and as a result of exposure to radioactive rays.

Leukocytosis with relative or absolute hypogranulocytosis occurs in acute leukemia; there are generally ulcerative lesions in the mouth with *B. fusiformis* and spirochetes in association. An interesting observation in this disease is that marked increase in white cells does not occur until the sore mouth develops. This peculiar blood reaction also occurs in conditions other than leukemia when these organisms are associated in ulcerations of the mouth and throat. While there is not proof that this reaction is a specific one, frequency of its occurrence would indicate that it is more than a coincidence.

EUGENE H. SMITH, Ogden, Utah.

ACUTE DISCHARGING EARS: INDICATIONS FOR OPERATIVE INTERFERENCE. CLARENCE A. VEASEY, Northwest Med. **28**:167 (April) 1929.

If the proper treatment for otitis media is given, the condition should heal in three weeks or less. If there is a persistent discharge, osseous necrosis in the mastoid is probably present and requires operation. The appearance of a small, nipple-like process on a perforated drum, noticeable slackening of the discharge

and postmastoid edema make operation imperative. The most serious complications are lateral sinus thrombosis, meningitis and labyrinthitis. Jugular bulb thrombosis is rare and occurs chiefly in children. Abscesses of the brain occur, for the most part, in cases of chronic otorrhea. The mastoid may perforate externally through the posterior zygomatic root, through the tip (Bezold's abscess) or even into the external auditory canal. Facial paralysis occurring during an attack of otitis definitely indicates operation. Veasey thinks that the x-rays are not of much value until late in the process. He describes fourteen pertinent cases.

SCOTT, Philadelphia.

ACUTE STREPTOCOCCIC LARYNGITIS WITH EDEMA; TRACHEOTOMY; CURE. M. CASSOUTE and POINSO, Bull. Soc. de pediat. de Paris **27**:87 (Jan.) 1929.

Dyspnea with stridor due to laryngeal obstruction is usually due to diphtheria. Sometimes, however, it may be due to other causes. A boy, aged 3½ years, had fever and a sore throat. Suddenly, the next day, he showed marked cyanosis and stridor. There was no membrane, and the throat was only slightly reddened. The condition was thought to be laryngeal diphtheria, and intubation was done. The index finger found an edematous epiglottis, and there was infiltration of the arytenoids and the superior part of the larynx. Only the smallest tube could be introduced; then a long tube was tried without success. A tracheotomy was done. The fever subsided in a few days, and after seven days the tracheal tube was removed. Every two days the boy was given injections of a vaccine to prevent bronchopneumonia. Four days after the removal of the tube, he was discharged cured. Examination of the exudate from the pharynx and from the larynx showed pure cultures of streptococci but no diphtheria bacilli. Severe acute laryngitis, not due to diphtheria, is encountered in measles, and may require intubation, and less commonly in primary laryngitis caused by staphylococci or streptococci. The severe edema in the latter makes intubation difficult, and even if the tube is properly inserted it does not give complete relief because of the edema of the mucous membrane. The proper procedure is to do a tracheotomy, which puts the larynx completely at rest. Tracheotomy, properly performed and in time, i. e., before the child is exhausted by repeated efforts at intubation, is not a serious operation and does not expose the child to possible complications any more than intubation does.

BENJAMIN, Montreal.

STREPTOCOCCI IN THE THROATS OF CHILDREN. HEDWIG HERZBERG, Monatschr. f. Kinderh. **43**:328 (May) 1929.

Of 177 patients in the Düsseldorf children's clinic, Herzberg made 2,200 cultures from the throat. Her observations agree well with those of American writers who state that the hemolytic streptococcus is a frequent inhabitant of the normal throat.

The nurslings had the lowest rate (from 4 to 28 per cent), and the children in the tuberculosis wards the highest (from 41 to 79 per cent). The author says that an average of 40 per cent of the children of from 2 to 15 years of age in this institution are hemolytic streptococcus carriers.

The influence of weather and climate was not as marked as one might expect. There was perhaps a slight increase during the cold, damp months of September through December, but nothing definite, and in many cases the increase was in the summer and the decrease in the winter.

There was no relation between the number of carriers and the occurrence of scarlet fever in the ward.

GERSTLEY, Chicago.

Diseases of the Skin

SOME SKIN DISEASES CAUSED BY INTERNAL DISTURBANCES. FOREST A. BLACK, Northwest Med. **28**:220 (May) 1929.

Skin diseases without definite etiology, such as pruritus, eczema, psoriasis or alopecia areata, can often be referred to an underlying systemic condition. Among

the conditions to be considered are tuberculosis, low grade pyogenic infections, hyperglycemia, endocrine imbalance, pregnancy, menopause, calcium deficiency, blood dyscrasias, alcoholism, cardiac disease and renal disease.

SCOTT, Philadelphia.

CONGENITAL ECTODERMAL DEFECT. H. MACKAY and A. M. DAVIDSON, Brit. J. Dermat. **41**:1 (Jan.) 1929.

Mackay and Davidson report four cases of this disorder and point out the fact that minor grades of the condition unquestionably pass unrecognized. The cases presented occurred in a woman, aged 32 years, and her two sons and one daughter aged 6, 11 and 13 years, respectively. The defects in each case were present from birth, and the abnormalities in the family group examined were uniform. The woman's mother, one sister, her grandfather and her great grandmother presented similar symptoms. There was marked hypotrichosis, especially of the hair of the mother's scalp. The eyebrows, eyelashes and lanugo hair were also involved in all of the group. All of the nails were dwarfed, roughened, thrown into ridges and presented hyperkeratosis of the nail-bed. No changes were noted in the teeth, and the integument apparently had its full complement of sudoriferous and sebaceous glands. Three photographs accompany the article.

WIEN, Chicago.

THE CHLORIDE CONTENT OF THE WHOLE BLOOD IN ECZEMA. N. BURGESS, Brit. J. Dermat. **41**:6 (Jan.) 1929.

Burgess reviews the literature indicating the possibility of disturbed chloride metabolism in eczema, and investigated the chloride content of the whole blood in cases included in this group and in certain other diseases of the skin. In his work the chloride content of the whole blood was estimated by the method of Whitehorn. Investigations were made in normal persons, persons suffering from acne, generalized pruritus and pemphigus, as well as in those with eczema. The estimations of the blood chlorides in all these conditions were within normal limits, and high or low values could not be correlated with any clinical type. In view of these observations Burgess states that there appears to be no indication for attempting to reduce the chloride content of the blood in the treatment of these diseases. Tables presenting the blood chloride values in five normal persons, ten patients with various dermatoses and twenty with eczema, accompany the article.

WIEN, Chicago.

POISONING BY THALLIUM ACETATE. Brit. M. J. **1**:712 (April 13) 1929.

A London coroner's jury returned a verdict of death from poison accidentally administered in the case of three brothers, aged 10, 7 and 5 years, respectively, who had been treated for ringworm of the scalp by the internal administration of thallium acetate at a hospital.

The value of this drug in the treatment of tinea capitis, based on its property of producing a total, though temporary, alopecia, was first recognized early in the present century by Sabouraud, but it was not until 1918, when Prof. R. E. Cicero discovered that by carefully assessing its dosage in terms of body weight he was able to prevent the severe toxic symptoms occasionally attending its administration, that the employment of thallium acetate became at all general. The dose recommended by Cicero, of 8 mg. per kilogram of body weight with a maximal dose for any patient, however heavy, of 0.3 Gm. has been found by dermatologists generally to produce satisfactory results. It is clear from the evidence at the inquest that the doses actually ordered for the three boys fell well within these limits. On chemical analysis, however, it was found that each dose of the solution administered contained from five to six times as much thallium acetate as was ordered in the prescription, a blunder which arose not from any carelessness in the actual dispensing, but from the fact that the hospital pharmacist had made a mathematical error in converting the amounts of the prescription from the metric to the apothecaries' measure.

ARCH. DERMAT. & SYPH.

CONGENITAL PEMPHIGUS APPARENTLY NOT OF SYPHILITIC ORIGIN. BRIAND, FONCAULT and MICHEL, Bull. Soc. de pédiat. de Paris, May, 1929, no. 5, p. 251.

The authors present a detailed case report of epidermolysis bullosa in an infant aged 2 months.

CLAUSEN, Rochester.

A CASE OF GENERALIZED LICHEN PLANUS CURED BY RADIATION OF THE AXILLA (PERI-ARTERIAL SYMPATHETIC RADIOTHERAPY). J. GOUIN and BIENVENUE, Bull. Soc. franç. de dermat. et syph. **36**:96, 1929.

In a child, aged 10, with lichen planus, the author obtained a cure by a single irradiation of the right axilla. He reiterates his former opinion that so-called spinal irradiation (medullary and radicular) is in reality irradiaton of the sympathetic system so far as the effects evoked are concerned. The present case is cited as proof of the hypothesis.

ARCH. DERMAT. & SYPH.

THE FINGER-NAILS AND TOE-NAILS OF NURSLINGS. HIROSHI SUGITA, J. Pediat. (Tokyo), March 20, 1929, no. 346, p. 479.

The author studied the physical development and chemical composition of finger and toe nails in ten normal infants for a period of about six months in each case. All infants were under 1 year of age. The conclusions are as follows: The finger-nails develop more rapidly than the toe-nails. Of the finger-nails, the fifth finger-nail develops most slowly, but all others develop at an almost equal rate. Of the toe-nails, the first one develops rather rapidly and the fifth most slowly, and the intermediate ones develop in a stepladder manner. The finger-nails grow at a uniform rate of about 2.1 cm. during the first year, with the exception of the fifth one, which has a rate of 1.8 cm. Of the toe-nails, the first grows about 1.6 cm. during the first year, while the fifth grows 0.9 cm. There is no difference between the right and the left feet. The total weight of all finger-nails during the first year is about 0.2 Gm., and that of the toe-nails, 0.1 Gm. As to the chemical composition, the analysis showed water content (12.32 per cent), nitrogen (13.24 per cent) and ash (0.89 per cent).

KATO, Los Angeles.

Surgery and Orthopedics

SCHLATTER-OSGOOD DISEASE: REPORT OF TWO CASES. A. N. WILSON, C. R. FISHEL and J. A. LAGASA, Northwest Med. **28**:134 (March) 1929.

This disease is believed to be an incomplete separation of the tibial tubercle, possibly caused by a violent contraction of the quadriceps, although some surgeons think that it is due to a low-grade infection, to endocrine disturbance or to a developmental anomaly. The disease is more common in boys than in girls and usually occurs during adolescence. Usually these patients may be treated by adhesive strapping, but occasionally the application of casts is necessary. Cases are reported, one in a boy, aged 12, and the other in a girl, aged 9.

SCOTT, Philadelphia.

PARALYTIC ILEUS AND HIGH INTESTINAL OBSTRUCTION: THEIR RATIONAL MANAGEMENT. MILLARD T. NELSON, Northwest Med. **28**:220 (May) 1929.

The author reviews some of the experimental evidence on this subject. A patient still vomiting thirty-six hours after operation should be suspected of having obstruction. Other symptoms are dehydration, thirst, tetanoid twitchings, rapid pulse, low temperature, a lowered blood chloride, high carbon dioxide-combining power and nitrogen retention. Haden and Orr consider a blood chloride as low as 400 a danger signal and advise large infusions of concentrated sodium chloride. The author gives 600 cc. of 3 per cent salt intramuscularly and 3 per cent salt with from 5 to 10 per cent dextrose intravenously. He washes

the stomach every four hours until it is clear. He cautions against giving sodium bicarbonate and also against too hurried jejunostomy.

SCOTT, Philadelphia.

TORTICOLLIS; REMOVAL IN EARLY LIFE OF THE FIBROUS MASS FROM THE STERNOMASTOID MUSCLE. H. LEROY VON LACKUM, Surg. Gynec. Obst. **48**:691, 1929.

Four infants with congenital torticollis with localized swellings in the sternocleido-mastoid muscles obtained marked relief after the removal of thick scar tissue from the muscle. Microscopically, this tissue consisted of connective and dense scar tissue in which muscle fibers occurred singly and in groups.

RICHARD A. LIFVENDAHL.

EIGHT CASES OF ACUTE INTUSSUSCEPTION IN INFANTS AND SOME OBSERVATIONS THEREON. J. DOUGLAS R. MURRAY, Brit. J. Child. Dis. **26**:83 (April-June) 1929.

In the course of a year the author had eight patients with acute intussusception under his care, all boys ranging in age from 3 to 22 months. Open reduction after laparatomy was the treatment in each case. There were two deaths, but no autopsies were obtained. As cardinal signs, the author mentions: (1) intermittent attacks of pain, (2) a tumor in the line of the colon and (3) the passage of blood and mucus per rectum. He does not regard vomiting as of diagnostic importance.

Theorizing on the etiology of the disease, the author states that Weeks and Delprat found that in the first year of life the amount of lymphoid tissue in the lower ileum is quite large and the lumen of the intestine proportionately small. Intestinal irritation due to dietetic errors may result in lymphoid hypertrophy and consequent intussusception in this area in particular.

LANGMANN, New York.

INTERNAL HERNIA IN AN INFANT AGED THREE WEEKS. T. TWISTINGTON HIGGINS, Proc. Roy. Soc. Med. **22**:651 (March) 1929.

The patient became jaundiced on the fourth day after birth. This condition continued till he was admitted to the hospital, at the age of 3 weeks, because of vomiting bile-stained fluid. Visible peristalsis of the ladder pattern was observed. The diagnosis was made of (1) icterus neonatorum and (2) obstruction in the small intestines. The roentgenologist reported, "Bismuth meal arrested just above the ileo-cecal valve." The infant was operated on and made an uneventful recovery.

WILLIAMSON, New Orleans.

BILATERAL OSTEOMYELITIS OF TIBIAE. E. A. CROOK, Proc. Roy. Soc. Med. **22**:899 (May) 1929.

A boy, aged 13 years, gave a history of pain and swelling of both ankles for six weeks which was thought to be due to rheumatism. When he was seen later by a surgeon, a diagnosis of suspected osteomyelitis was made. During an exacerbation of symptoms, a rising leukocyte count and a more positive roentgen examination made the diagnosis clear. At operation, a cavity was found containing thick white pus at the lower end of each tibia. Examination of the pus showed the presence of *Staphylococcus aureus.*

WILLIAMSON, New Orleans.

ANATOMIC OBSERVATIONS IN TWO CASES OF PYLORIC STENOSIS AFTER OPERATION. P. LEREBOULLET, AUROUSSEAU and SAINT-GIRONS, Bull. Soc. de pédiat. de Paris **27**:69 (Jan.) 1929.

The authors were able to make a postmortem examination of two infants who had pyloric stenosis and who had been operated on (extramucous pylorotomy).

They had both made uninterrupted postoperative recoveries. One died thirteen days after operation of severe diarrhea, and the other died four months after operation of tuberculous bronchopneumonia. In both cases, the operative incisions could easily be seen. There was a deep depression of 0.5 cm. which was about 0.5 cm. wide at its widest point, and there was practically no scar filling in the defect. These observations are quite different from those of Martha Wollstein and of Fredet, Lesne and Coffin who found complete filling in of the operative incision in their cases of postoperative pyloric stenosis that came to necropsy. This discrepancy may be due to some difference in the technic of the operations. The patient is cured, apparently, whether the cut surfaces of the muscular layer grow together or not, and the authors suggest that the mere cutting of the muscular layer and thereby severing the nerve endings which supply the muscular tissue effect the cure of the condition. This corresponds with Bard's views on the pathogenesis of congenital hypertrophic pyloric stenosis.

BENJAMIN, Montreal.

KLIPPEL-FEIL SYNDROME WITH MARKED VERTEBRAL ANOMALIES; REPORT OF A CASE. ALBERT MOUCHET and ROEDERER, Bull. Soc. de pédiat. de Paris **27**:101 (Jan.) 1929.

The authors report the case of a girl, aged 9 years, whom they first saw at the age of 5 years, with a short neck, the chin touching the sternum, the right shoulder raised and marked kyphosis. There was a small depression at the level of the spinous process of the sixth cervical vertebra and a sharp scoliosis between the sixth cervical and the first dorsal vertebrae. The most marked feature was the stiffness of the neck; the head was held forward and could hardly be moved in any direction. The hair line was low. The right scapula was smaller than the left, and the right shoulder was higher. The right upper eyelid was ptosed. She was mentally backward.

Roentgenologic examination showed: In the anteroposterior view, the first dorsal vertebra was slightly polygonal; above this was a mass representing the lower cervical vertebrae, in which the lateral processes appeared united; above this, there was a vertebra with a spina bifida. Above this, the other vertebrae could not be seen because of the shadow of the lowered chin. In the lateral view the bodies of the atlas and axis were united, and the body of the atlas itself was poorly differentiated from the occipital bone; a third vertebral body was flattened; then there was a long body divided transversely by a little line which represented a rudimentary disk—in all, three vertebral masses in which one could distinguish five vertebrae. The spinous processes of the atlas and axis were large and curved. The third vertebra had a large straight spinous process and the two lower united vertebrae had their spinous processes united so that only the tips were separated. Under this, the spinous process of the first dorsal vertebra was long. The child had worn a Minerva jacket since the age of 2 years, which lessened the deformity. The neck was slightly extended, the head was raised, and movement of the neck was made easier.

BENJAMIN, Montreal.

PRECORDIAL THORACECTOMY FOR ADHERENT PERICARDIUM. R. WORMS and R. M. D'AUBIGNE, Bull. Soc. de pédiat. de Paris **27**:219 (May) 1929.

Of sixty-three cases of adherent pericardium in which surgical treatment was given and which were reported in the literature, only sixteen occurred in children under 15 years of age. In the author's case, that of a boy, aged 11 years, Brauer's operation was followed by excellent functional results. The pericardium immediately at the operative site was not adherent. Deformity of the chest occurred at once and remained unaltered for three months. Auscultatory signs were not changed, and the orthodiagrams of the heart showed no decrease in size.

CLAUSEN, Rochester, N. Y.

SURGICAL TREATMENT FOR ADHERENT PERICARDIUM. MERLE D'AUBIGNE, Bull. Soc. de pédiat. de Paris **27**:225 (May) 1929.

Delorme's operation, the freeing of intrapericardial adhesions, is possible only in early cases. Schmieden's operation, favored in Germany, consisting of total ablation of both adherent leaves of the pericardium over the left ventricle, carries a high mortality. Brauer's operation, precordial thoracectomy, appears to afford quite as much relief and is attended with relatively little difficulty. It is indicated whenever the signs indicate adherent pericardium, and has been of help even in cases in which no adhesions were found, by removing from the myocardium the burden of moving the precordial thoracic wall. Of sixty-four cases described in the literature, benefit was derived in fifty-seven; only thirty-three of these were followed longer than three months. Among the patients not benefited, four deaths occurred, either immediately or during the first preoperative week; and in five cases the condition continued without relief of symptoms. The other twenty-four cases showed improvement, which was moderate in nine and not consistent in fifteen. All failures to improve occurred in patients presenting the symptoms of extremely advanced cardiac failure.

Among sixteen children under 15 years of age, there was one operative death and ten good results; six patients were followed for two, three, four and five years.

CLAUSEN, Rochester, N. Y.

POTT'S DISEASE WITH PARAPLEGIA; REPORT OF A CASE. B. CARDELLE, Bol. Soc. cubana de pediat. **1**:179 (April) 1929.

A case of tuberculosis of the spine in a girl, aged 29 months, was complicated by paraplegia. There was loss of motion in the limbs and in indifferent ability to appreciate sensation. The Babinsky sign was strongly positive. The possibilities of both medicinal and operative treatment are discussed, but Cardelle believes that the prognosis is hopeless.

SANFORD, Chicago.

CONSERVATIVE TREATMENT IN PNEUMOCOCCUS EMPYEMA OF EARLY CHILDHOOD. RICHARD GROSSER, Monatschr. f. Kinderh. **43**:222 (May) 1929.

The author reviews the various treatments for empyema and in a report of seven cases states his belief that the best results are obtained by repeated aspiration. As an auxiliary to this treatment, he advises irrigation with a solution of ethylhydrocuprein hydrochloride, according to the method of R. Gralka.

The technic is simple. With a 20 cc. syringe, as much of the pus as possible is aspirated. Using the same syringe, one irrigates the cavity with from 100 to 200 cc. of a 0.5 per cent freshly prepared solution of ethylhydrocuprein hydrochloride. After repeated aspiration, one leaves a 5 per cent solution of the hydrochloride in the cavity in amounts depending on the body weight, but never more than 0.5 Gm. (10 cc. of the 5 per cent solution). The treatment lasts for from one to six weeks and ceases when the amount of pus obtained by aspiration is not more than from 1 to 2 cc. The writer is definite in his conclusion that the irrigation with ethylhydrocuprein is a great improvement over the old technic of simple repeated aspiration.

GERSTLEY, Chicago.

PARANEPHRIC ABSCESS. ANNEMARIE LABAND, Monatschr. f. Kinderh. **43**:237 (May) 1929.

The author distinguishes between perinephritis (inflammation of the fibrous capsule of the kidney), epinephritis (inflammation of the fatty capsule) and paranephritis (inflammation of the retroperitoneal portion of the capsule).

This is the report of the case of a child who entered the hospital with symptoms of severe cystitis. The fixation of the right leg pointed first to the hip joint and then later to the reddened and tender area near the right kidney.

Aspiration and later operation showed an abscess in the capsule of the kidney which on postmortem examination proved to be a paranephric abscess.

GERSTLEY, Chicago.

Miscellaneous

SUMMARY OF PROVISIONAL DEATH, AND INFANT MORTALITY FIGURES IN THE BIRTH REGISTRATION AREA: 1928. Department of Commerce, Bureau of Census, July 22, 1929.

The birth rate for 1928 was 19.7 as compared with 20.7 for 1927, in the birth registration area. The death rate was 12.3 as compared with 11.4 in 1927. The infant mortality rate for 1928 represents an increase as compared with 1927, the rate being 68 for 1928 and 64.6 for 1927.

SANFORD, Chicago.

USES AND ABUSES OF ULTRAVIOLET LIGHT. CLARENCE A. SMITH, Northwest Med. **28**:261 (June) 1929.

Among the conditions in which improvement is obtained by ultraviolet therapy, Smith mentions rickets, tetany, spasmophilia, osteomalacia, anemia and malnutrition. It is also helpful in tuberculosis of the glands, intestines, peritoneum, bones and joints. Patients with recurrent colds and chronic bronchitis are often improved by its use. Nasal applications are of benefit to some asthmatic patients. Local irradiation is useful in some cases of psoriasis, and chronic eczema can sometimes be improved by it. Ultraviolet rays are highly bactericidal, and local application quickly relieves many infectious processes.

Among the conditions in which this form of therapy does harm are acute tuberculosis, diabetes and hyperthyroid states. Overexposure causes anorexia, fatigue, restlessness, insomnia and loss of weight. In rickets, overexposure may cause overcalcification of the long bones and arrest of their growth. Overexposure is said to reduce the bactericidal properties of the blood. Caution is given against unsupervised treatment.

SCOTT, Philadelphia.

THE DECREASE IN MATERNAL AND INFANT MORTALITY IN OREGON. FREDERICK D. STRICKER, Northwest Med. **28**:118 (March) 1929.

Infant deaths in Oregon decreased from 63 per thousand in 1919 to 47 per thousand in 1927. This is compared to 65 per thousand for the United States as a whole in 1927. Methods of decreasing both maternal and infant mortality are discussed.

SCOTT, Philadelphia.

A STUDY OF THE RELATION BETWEEN MENTAL AND PHYSICAL STATUS OF CHILDREN IN TWO COUNTIES OF ILLINOIS. G. A. KEMPF and S. D. COLLINS, Pub. Health Rep. **44**:1743 (July 19) 1929.

Approximately 5,000 children were examined both physically and mentally. The prevalence of physical defects among children of low intelligence quotient was compared with that among children of average and high intelligence quotient. The average number of physical defects decreases as the intelligence quotient increases. This tendency seems to be independent of race, language and other similar factors. This result might be due to several factors: (*a*) The handicap due to physical defects may result in slower mental development. (*b*) The children who are slow in mental development may tend to come from families whose innate or constitutional physical characteristics are also below the average. (*c*) The slower physical and mental developments may both be the result of other factors with which both are correlated, such as adverse conditions of various kinds.

SANFORD, Chicago.

SWELLING OF LEFT THUMB. E. A. CROOK, Proc. Roy. Soc. Med. **22**:642 (March) 1929.

A girl, aged 12 years, reported that she had had a painless swelling of the left thumb and a painless fluctuating swelling of the right cheek for several weeks. The roentgenogram pointed to tuberculous dactylitis. The Wassermann reaction was negative. Seven months later, roentgen examination suggested enchondroma rather than dactylitis. Eleven months later, roentgen examination was in favor of dactylitis. No organisms were found in the fluid which was aspirated from the cheek.

WILLIAMSON, New Orleans.

PERICARDIAL PUNCTURE VIA THE EPIGASTRIUM. A. B. MARFAN, Bull. Soc. de pédiat. de Paris **27**:227 (May) 1929.

Having read the essays of Larrey and Jaboulay on incision of the pericardium via the epigastrium, Marfan in 1911 first carried out puncture by this route. The patient should not be flat on his back, but should be half reclining. The deformity of funnel-chest and abdominal distention make the procedure difficult unless one uses a curved trocar. In case of marked deformity, it may still be possible to enter the pericardial sac if one introduces the trocar into the right or left costoxiphoid angle, pointing the needle toward the median line. The exploration of localized pericardial effusions is discussed.

CLAUSEN, Rochester, N. Y.

POISONING WITH "META" IN CHILDHOOD. P. GAUTIER, Bull. Soc. de pédiat de Paris **27**:255 (May) 1929.

"Meta," a solid fuel, is a polymer of acetaldehyde differing from paraldehyde. In warm-blooded animals, 0.5 Gm. per kilogram causes disturbances of the pulse, dyspnea, convulsions, trismus and opisthotonos. The lethal dose for the dog is about 0.5 Gm. per kilogram. In two cases described by Gautier, pain in the stomach, pallor, convulsions and strabismus occurred, and during convalescence a gait suggestive of alcoholism, "nervousness" and clumsiness.

CLAUSEN, Rochester, N. Y.

DEFECTIVE CHILDREN OF PRIMARY SCHOOLS IN THE PROVINCE OF BUENOS AIRES. CARLOS S. COMETTO, Bol. Inst. Internac. Am. de proteccion a la infancia **2**:389 (April) 1929.

According to statistics covering a school population of 51,361, 13.3 per cent of the children were defective. The children in the 6,870 cases mentioned were classified as follows: 429 stutterers; 2107 with defective pronunciation; 227 markedly deaf; 1,650 insufficient in attention and in memorizing or imaginative activities; 1,096 restless and undisciplined; 667 apathetic and asthenic; 554 amoral; 140 with various tics; 185 epileptic, and 1,602 who found difficulty in reading mechanically.

It would seem to the reviewer that in at least three of the foregoing groups the child is not necessarily defective. The difficulty might be environmental or might even lie with the teacher.

The writer concludes that special schools should be founded for mentally and physically handicapped children, as well as special classes annexed to common schools for less defective children. This necessitates special training for the teachers to enable them to take charge of such schools and classes. Technical courses for teachers of defective children should also be organized.

LESLIE, Evanston, Ill.

BRAZILIAN COUNCIL FOR THE ASSISTANCE AND PROTECTION OF MINORS. OLINTO DE OLIVEIRA, Bol. Inst. Internac. Am. de proteccion a la infancia **2**:398 (April) 1929.

The council of minors, annexed to the Department of Justice and the Interior, exists for the purpose of studying and solving all problems concerning the child and adolescent; fighting all social evils that affect the child in particular, endangering its health, life and morals; promoting the protection of the neglected, the weak and the sick child; organizing this protection, encouraging the creation of institutes and placing the neglected children in families or homes; supervising the children in the streets and in all schools, factories and workships; aiding the action of the judge acting in behalf of minors; reporting to the Department of the Interior and to the said judge the faults and abuses committed against children, and constituting the Brazilian Federation of Children's Welfare Associations.

The council has thus far constituted three permanent committees, one of which, that of study and propaganda, is beginning to develop a wide plan of work.

LESLIE, Evanston, Ill.

INFANT MORTALITY AND BIRTH RATE IN BAVARIA. AUGUST OETTL, Monatschr. f. Kinderh. **43**:309 (May) 1929.

It has long been known that the infant mortality in southern Germany has been higher than it should be and has not decreased in the same proportion as in other lands.

The author has made an ethnologic survey and finds that there are four racial stocks in this land: Bavarian, Swabian, Frankish and Alemanic. Unquestionably, the highest mortality occurs among the Swabians and Bavarians. Although the birth rate among the Bavarians is higher than in the other races, he believes that the high mortality in addition to the usual nutritional disturbances is due largely to a certain racial weakness.

GERSTLEY, Chicago.

RESEARCHES ON IRRADIATED ERGOSTEROL. A. HOTTINGER, Ztschr. f. Kinderh. **47**:341 (March 23) 1929.

The activity of big doses of optimal, irradiated ergosterol on the metabolism was studied by the determination of calcium and phosphorus balances and by urinalyses in experiments comprising forty-six metabolism periods in seven children and two dogs. Two types of reaction could be distinguished: that of normal breast-fed and bottle-fed infants, including those convalescent from rickets, and that of infants with rickets or with tetany. In normal breast-fed and bottle-fed infants, the amount of calcium eliminated in the urine increased sharply within the first twenty-four hours after the exhibition of D factor. The calcium balance was diminished and might even become negative through simultaneous loss in stool and urine. The same condition was found, less markedly, in the course of the phosphorus metabolism. It was produced, perhaps, by an initial negative deviation of the mineral threshold that might arise from a positive balance. The urinalyses indicated a transient shift of the metabolic rate toward the acidotic side in the first days. In cases of rickets, the great and immediate increase of the calcium balance by the sparing of the outgo in urine and stool was impressive; within the first twenty-four hours after the exhibition of D factor, the elimination of calcium in the urine diminished quickly. The phosphorus balance improved slowly, chiefly because of better resorption from the intestine. Rachitic acidoses continued to be demonstrated for a long time and disappeared completely with definite healing. In tetany as in rickets the calcium balance was increased, but at the same time the body, under the activity of D factor, retained less phosphate. By an experiment on rachitic dogs to compare the spontaneous process of healing and the process of repair under the activity of D factor, it was shown that D factor not only acted on the mineral balance favorably but also had a local structure-giving power that affected the bones.

EMERSON, Boston.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Annual Meeting, May 28, 1929

MAURICE L. BLATT, M.D., *President, in the Chair*

THE POLYMORPHONUCLEAR COUNT IN THE NEW-BORN. PRELIMINARY REPORT. INAUGURAL THESIS. Presented by DR. H. N. SANFORD.

This paper was published in full in the August issue, p. 271.

DRY CLINIC: CASE REPORTS

ERYTHEMA NODOSUM. Presented by DR. JOSEPH GREENGARD.

Adelle S., white, aged 9, was admitted to the Municipal Contagious Disease Hospital on March 22, 1929, with a diagnosis of convalescent scarlet fever. Her younger brother entered on the same day with a typical case. Her physician said that the date of the onset of her illness was March 19, 1929. The temperature on admission was 101 F., the pulse rate 120 and respirations 24. No rash, desquamation or any other evidences of scarlet fever were noted at the initial examination. The urine was entirely normal; the white blood cell count 11,400, and culture of material from the throat did not show diphtheria bacilli. A blood plate culture from the throat was positive for hemolytic streptococci.

A few days later she developed acute otitis media in the left ear, which was opened on April 9; a hemorrhagic purulent material drained from it. Except for the otitis media, the course was uneventful, an occasional slight rise in temperature occurring, until April 16, when the temperature went up to 102 F., and she seemed much worse. On this date the pharynx was found to be acutely inflamed, with a thin, grayish, patchy membrane present over the right tonsil. On the basis of this observation, the resident physician gave her 10,000 units of diphtheria antitoxin immediately. The following day, April 17, a typical scarlatinal eruption was present, which ran its usual course accompanied by desquamation and a typical condition of the tongue and throat. .

On April 19, the child complained of pain in the right leg, which was attributed to the antitoxin given three days previously. The following day she complained of pain in the arms, but on examination no tenderness, swelling or redness of any of the joints was noted. During this period she continued to have an irregular temperature varying from 99 to 100 or 101 F. daily, and the left ear was still draining.

On May 1, a typical erythema nodosum appeared. Three raised, bright red areas, ovoid in shape, varying from 1 to 3 cm. in diameter, were present over the right tibia, one smaller area near the right external malleolus, and two similar areas over the left anterior tibial surface. They were firm and elastic on palpation and were associated with a moderate edema of the surrounding skin, with definite subjective pain and marked tenderness on pressure. There were no other similar lesions elsewhere over the body, and no involvement of the joints was noted. No appreciable change in the temperature or in the general condition was noted with the onset of the lesions. They ran their typical course, going through the various color changes of a bruise, and by May 14 were entirely faded.

On May 1, as soon as the eruption was noted, a Pirquet test was done, which was negative after twenty-four and forty-eight hours. On May 10, the Pirquet test was repeated and was again entirely negative. On May 12, an intradermal tuberculin reaction was performed, 0.1 mg. of old tuberculin being used. This

reaction was entirely negative. On May 15, the Mantoux reaction was repeated, 1 mg. of old tuberculin being given intradermally. This reaction was also entirely negative. In these tests two distinct tuberculins were used, both of which had given definite positive reactions within the past few months.

On May 8, the child's temperature began to show wider fluctuation, varying from normal or 99 F. in the morning to 102 in the evening, and distinct mastoid tenderness was noted. During the next few days these symptoms increased and operation was deemed advisable, a simple mastoidectomy being done on May 15. A few days later the right drum showed evidences of inflammation, purulent otitis media finally occurring in the right ear.

On May 19, the typical lesions of erythema nodosum, which had completely disappeared, recurred over the anterior tibial surfaces. They were similar in every respect to the initial eruption, occupying almost the idential areas, and ran a similar course. On May 27, they had almost completely faded. On this occasion, also, no involvement of the joints was noted. There was no marked change in the temperature curve with this second invasion, an irregular temperature up to 100 or 101 F. persisting.

This recurrence of the lesions is of interest since it took place four days after intradermal administration of 1 mg. of old tuberculin. Ernberg was able to produce recurrences of erythema nodosum by the subcutaneous administration of tuberculin. In this case, however, since no positive allergy to tuberculosis was present, it seems unlikely that the injection of tuberculin injection was a factor in producing a recurrence. At about the same time a surgical procedure was done in an infected area, and it seems more possible that the recurrence was due to absorption from this region.

DISCUSSION

DR. H. E. IRISH: The term erythema nodosum, which means red nodule, has come to be applied to a variety of nodules whether white or purple. The white tendinous and aponeurotic nodules, as well as purpuric nodules, are probably due to the same etiologic factor and have been termed nodosa rheumatica. No wholly satisfactory term exists for these nodules, whether they are tuberculous or anaphylactic in origin.

PERITONSILLAR ABSCESS IN AN INFANT AGED THREE WEEKS. Presented by DR. CRAIG BUTLER.

Peritonsillar abscess is rarely mentioned in pediatric texts. Dr. Kerley stated in his book that he has seen but one patient under 6 years of age. The literature contains few reports of the condition in infancy, the youngest patient found being an infant aged 6 months. The following case in an infant aged 3 weeks is therefore considered worthy of report.

Marilyn H., the second child of healthy parents, was born on April 11, 1929. She left the hospital on the fourteenth day after birth, having regained her birth weight and no abnormality having been noted. The mother had noticed that her breathing during nursing was noisy and rather difficult. After a few quiet days at home, she became increasingly fussy. On the twenty-first day she was quite ill, nursed poorly, and the mother noted, for the first time, a swelling on the right side of the neck. A physician found a rectal temperature of 100 F., a red throat and cervical adenitis. The infant cried all night, and in the afternoon of the next day presented the following picture: She was well nourished, but in evident pain; the temperature was 99.8 F. rectally. She noursed well, but allowed the milk to escape from the mouth. The right anterior cervical glands were greatly swollen. The right side of the soft palate was swollen and red, the uvula lying against the left side of the throat. The swelling was tensely fluctuant.

The infant was taken to the West Suburban Hospital and the abscess opened without anesthesia by Dr. R. H. Good. Much greenish-yellow pus escaped under great pressure. No swelling of the retropharyngeal wall was present. Recovery was rapid and uneventful. Staphylococci were recovered from the pus.

DISCUSSION

DR. ARCHIBALD L. HOYNE: The reference to peritonsillar abscesses in young children recalls to me that a number of times I have seen children who were thought to have laryngeal diphtheria who actually had retropharyngeal abscesses. The youngest child with a case of this sort was an infant aged 4 weeks who was sent to the Municipal Contagious Disease Hospital with a request for intubation. The child was blue, but as soon as the abscess was opened it became practically normal.

One thing should be kept in mind in connection with cases of this type, and that is that as soon as the mouth gag forces the jaws apart, the patient often stops breathing. Frequently the abscess must be opened quickly if death is to be prevented.

DR. JOSEPH BRENNEMAN: To my mind there are three definite inflammatory entities of the throat accompanied by suppuration. One is a retropharyngeal abscess that rarely occurs after the second or third year of age. The second is the ordinary peritonsillar abscess that is rare under 5 or 6 years of age. The third type not infrequently occurs in children, commonly before the peritonsillar and after the retropharyngeal period. In this type an abscess forms back of the tonsil and pushes it forward so that it can be seen well, instead of forming a maximum swelling in front of and mesial to the tonsil. These abscesses usually rupture spontaneously and are often best left untreated.

I should like to know whether the otolaryngologist made the incision in this case in front of, or in back of, the tonsil.

DR. HENRY E. IRISH: Pathologically, retropharyngeal and paratonsillar abscesses originate in glands, while peritonsillar abscesses, or "quinsy," are due to suppuration occurring after cellulitis. The peritonsillar abscess is said not to occur in patients under 3 years of age, as a rule. This winter I had an exception to that rule in a child aged 6 months with an abscess that occurred at the fauces. The anatomy has been well described by Heiman (Parapharyngeal Abscess, *Am. J. Dis. Child.* **10**:107 [Aug.] 1915), and the peritonsillar abscesses are the deep variety which fail to rupture into the throat and have to be opened from the outside because they are exceedingly deep.

DR. CRAIG BUTLER: The uvula was pushed well over, and the crest of the swelling was above and anterior to the tonsil. Dr. Good, the surgeon, said that the usual incision for peritonsillar abscess was made, i.e., a little above and in front of the tonsil.

FOREIGN BODY IN THE CHEST. Presented by DR. ARCHIBALD L. HOYNE.

On Jan. 17, 1929, a girl, aged 3 years, was sent to the Municipal Contagious Disease Hospital with a request for intubation. At the time of admission, the patient's temperature was 99.6 F. by rectum. The only statement in regard to the history was that respiration had been difficult for four days. Aside from some moist râles in the chest and impaired respiration, no physical signs were noted. Five thousand units of antitoxin were given, although the admitting physician concluded that the child did not have laryngeal diphtheria but was suffering from an enlarged thymus. A culture was later reported negative for diphtheria. On the following day, it was noted that with expiration a small object could be seen moving up against the wall of the chest in the vicinity of the clavicle to the left of the sternum. A roentgenogram was made, and this disclosed an object which resembled a nickel and appeared to be located to the left of the trachea. On communicating with the family it was learned that about four months previously the child had been suddenly seized with a severe coughing spell, and that from time to time during the next few weeks she had had severe attacks of coughing. On two or three occasions bronchoscopy had been resorted to, and the esophagus had been examined. Negative results had been reported. No roentgen examination had been made. When the case had proved not to be of a contagious nature, the family had moved the patient to a private hospital. While the child was at the Contagious Hospital no intubation was done, nor was it believed that a tracheotomy was advisable.

Some of the special points of interest in this case are that although a foreign body was distinctly discernible to the naked eye, it had not been observed prior to the patient's admission to the Contagious Disease Hospital. Moreover, no roentgen examination had been resorted to. How a foreign body reached this location was a matter for conjecture. It was too large to have been in the larynx, and it seems doubtful that it sloughed through the esophagus.

In all cases of difficult respiration in children, a number of questions arise in connection with the diagnosis. Most of them are rare conditions, but they may be encountered from time to time. Not long ago, a child sent to the Children's Memorial Hospital for intubation was found to be suffering from a mediastinal tumor.

Other conditions to be considered as causing embarrassed respiration are enlarged lymph glands, tracheobronchial diphtheria with no membrane in the throat, asthma, edema of the glottis and, rarely, influenzal meningitis. The possibility of a foreign body being located in the larynx or the trachea should be thought of and eliminated. Close observation of the patient is frequently of as great value as instrumental examination.

DISCUSSION

Dr. Philip L. Aries: An infant, aged 11 months, presenting a clinical picture somewhat similar to the one Dr. Hoyne discussed, was recently under my observation. The family physician, with whom I saw the patient, believed that the child had laryngeal diphtheria. The physical signs, however, were those of bronchial asthma. The roentgen examination of the chest revealed a faint but definite round shadow 1.5 cm. in diameter just below the clavicles. The original interpretation was that a disk-shaped wooden or rubber foreign body was lodged in the esophagus with the flat surface presenting on the anteroposterior roentgenograms. Esophagoscopy and bronchoscopy were then performed, but no foreign body could be visualized. After studying a series of films, Dr. Nathan Zeitlin diagnosed this shadow to be the ossification center of the manubrium sterni.

In the meantime the patient had recovered from the dyspnea. Since then, however, he has had more attacks of bronchial asthma, and according to skin tests is sensitive to several proteins.

Dr. Joseph Brenneman: This case recalls a similar one in a patient whom Dr. Krost and I saw several years ago, and I should like to know whether any purpuric spots were observed in this case.

In our case the child had something that looked like angioneurotic edema with purpura, and developed an acute abdominal condition with a complete obstruction. We could definitely feel a mass in the upper right quadrant. The child vomited, had reversed peristalsis, and finally an acute dilatation of the stomach. We inserted a continuous stomach tube, and ultimately the child made a complete recovery. With the purpuric spots, angioneurotic edema and the acute abdominal pain and obstruction, we thought of the case as belonging in the Henoch's purpura class.

Dr. Philip L. Aries: No purpuric spots were observed in the case I reported.

Pneumonia in New-Born Infants. Presented by Dr. Isaac A. Abt.

During the last few years, a number of cases of pneumonia in new-born and very young infants have occurred in my hospital and private practice. I desire to present a few points on the pathology and etiology in this disease group.

There is a significant difference between the thorax of children and that of adults. In children, the ribs lie more transversely and less slanting than in adults. The diaphragm exerts a powerful pull on the thorax. The bases of the lungs feel the influence of this strain. Consequently, localization of pneumonia in the more dependent portions of the lung relatively seldom occurs in contradistinction to the apical infiltration of adults.

The bronchial tubes in the lungs of children lie in two different planes: those which take a direction backward toward the spine and those which extend forward toward the sternum. The dorsal ones are shorter and seem to have a closer

connection with the main bronchi. Those which take a forward direction are more angular and have less direct connection with the main bronchi. This arrangement explains the greater frequency of aspiration pneumonias in the dorsal branches.

In measles and influenza the preterminal branches are more frequently involved, while in whooping cough the terminal bronchioles are affected; this explains the common occurrence of bronchiectasis following pertussis.

It has been commonly assumed that the elastic tissue, even in early childhood, has something to do with the elasticity of the lung, but it has been shown that this tissue has little to do with respiratory movements. In new-born infants, the elastic fibers are absent. They develop later with the functional expansion of the lung. The smooth muscles of the bronchi which develop at birth have to do altogether with the movements of the bronchi in both respiratory phases.

Another interesting point is the interacinar septum. One wonders how pneumonia gets from one acinus to another, from one alveolus to another, but it has been decided that these acini communicate with one another by tiny pores, which are just large enough to admit infectious material from one to another. These tiny communicating passages are known as Kohn's pores. When a bronchial branch is obstructed, the pulmonary tissue thus supplied becomes atelectatic. A number of acini together constitute a pulmonary lobule. These lobules are separated by interlobular septums which contain no pores. Obstruction of the main bronchus to the main lobule leads to atelectasis. It is obvious that pneumonic infection may extend from one acinus to another through these minute pores.

The viscosity of the fluid contained in the bronchi in infants is not much less tenacious than in adults, and in the minute bronchi this obstructs them and readily disposes to atelectasis. In aspiration pneumonia, this is probably one of the chief causes. Not a few children are born with aspiration pneumonia and show evidences of it during the first days of life. Many infants with respiratory disease who come to autopsy show liquor amnii in the bronchi, and many of those who develop pneumonia show liquor amnii, lanugo hairs and other foreign detritus that would be found in the liquor.

The narrow bronchi of infants are obstructed by minimal quantities of mucus, and this explains the frequency of extensive atelectasis in the young. Atelectasis causes increased tension in the adjacent tissue, which leads to localized emphysema. The alveolar walls of this emphysematous tissue may rupture and lead to pneumonia or empyema.

Not all pneumonias of the new-born infant are due to aspiration. Some are definitely infectious, occurring from some error in the obstetric technic. Epidemics of infectious infantile pneumonia are not rarely seen in hospital wards. In measles, the preterminal bronchi seem to be involved. The infection spreads to the respiratory bronchioles and then to the acini; then a confluent pneumonia occurs. It is well recognized that pneumonia occurs frequently with the exanthems.

Other forms of pneumonia occur in early life, not infrequently the types due to streptococci or staphylococci. Not long ago I saw a new-born infant with well developed pneumonia, multiple abscesses of the lungs and staphylococcic empyema. Not infrequently a pyopneumothorax is seen, and sometimes a chylothorax is encountered.

Empyema may occur in very young infants, and those who are connected with a service for new-born infants in a hospital will have observed at least a few cases. In the old days, when infection was rampant among both mothers and infants, infantile empyema was much more common, but even now it occurs following many different diseases. A certain number of cases are secondary to pulmonary infection of pneumococcic, streptococcic or staphylococcic origin.

One point I encountered in my reading was that pneumococcic infections, according to immunologic theories, should be rare in new-born infants. It is contended that no child can be infected by the pneumococcus until he has been sensitized to it; theoretically at least, this infection should be rare in the new-born infant.

SPASMOPHILIA: CASE REPORT. Presented by DR. C. G. GRULEE.

Dolores, a white infant, aged 2 months, was admitted to the hospital on April 8, 1929, because of convulsions, which were first noticed a month before admission. The convulsions would occur in a series of about forty-eight hours' duration, every seven to eight days, with a convulsion every hour, usually lasting one minute. The attack present at the time of admission had lasted three days. There had been no previous illnesses. The delivery was normal and at full term. The infant was given breast milk and complementary feedings for the first two weeks, after which the breast milk was inadequate, and a simple whole milk formula was given. For two weeks previous to admission, the infant was given Eagle Brand Condensed milk. No cod liver oil had been given. The family history was not significant.

On examination, the infant appeared well nourished, with good tissue turgor. Convulsions lasting from one to one and one-half minutes were observed. At the

Results of Laboratory Examinations

Blood

Date	Hemoglobin, per Cent	Red Cells	White Cells	Neutrophils	Small Mononuclears	Large Mononuclears	Eosinophils	Basophils
4/ 8/29	50	3,130,000	15,150	38	52	9	1	—
4/15/29	79	3,460,000	9,250	26	53	3	19	—
4/24/29	69	3,800,000	10,200	32	60	6	1	—
5/ 1/29	72	4,200,000	9,850	44	45	8	2	1

Urine

Date	White Cells	Albumin	Casts	Acetone
4/ 9/29	90	+	None	—
4/10/29	400	—	None	—
4/12 to 4/20	5 to 20	—	None	—
4/23 to 5/15	normal	..	.....	..

Spinal Fluid

Lange	000 111 000
Wassermann reaction	Negative
Ross-Jones	+
Cells	0
Sugar	42.1 mg.

Electrical Irritability

4/12/29 cathrodal opening contraction at 2.5 milliamperes
4/24/29 cathrodal opening contraction at 5.5 milliamperes

Date	Blood Calcium, Mg.
4/ 9/29	5.8
4/16/29	7.9
4/22/29	8.3
5/ 1/29	8.9
5/ 6/29	8.7
5/14/29	9.4

beginning of the seizure, the head rotated to the left, and there was a nystagmus to the left. The right side remained passive at first, but was involved later. Respiration was rapid and irregular during a paroxysm, but would be of the Cheyne-Stokes type immediately afterward. The parietal bossae were abnormally prominent. A marked rosary was present; otherwise, the chest and abdomen were normal. The deep reflexes were slightly exaggerated. Marked Kernig and contralateral signs were present. Chvostek's and Trousseau's signs were not obtained. The temperature was 104.8 F. on admission.

The convulsions were controlled by chloral hydrate, and once ether was necessary. The treatment consisted of calcium lactate, 15 grains (0.9 Gm.) every four hours, 3 drops of a preparation of irradiated ergosterol three times daily, and ultraviolet light therapy. The temperature dropped from 104.8 F. to normal within the first thirty-six hours; the elevation in temperature was thought to have been due to pyelitis, as the urinary symptoms improved at this time. The convulsions were frequent during the first two days but were controlled after that. A rise in temperature on May 3, 1929, which lasted for four days, due to an infection of the

upper respiratory tract, seemed to influence the blood calcium at that time. The results of the laboratory examinations are shown in the accompanying table.

Roentgen examination of the extremities did not reveal any changes in the bones.

ACUTE APPENDICITIS; HERPES ZOSTER; ANGIONEUROTIC EDEMA. Presented by DR. I. M. LEVIN.

L. H., a well nourished boy, aged 14, was first seen on Aug. 13, 1928, with a history of urticaria and angioneurotic edema of two months' duration. He was treated with saline cathartics, alkaline baths and a restricted diet, all fruit being eliminated except oranges, and was given ephedrine sulphate solution, 10 minims (0.6 cc.) every four hours, with prompt relief.

On the morning of March 28, 1929, he again had a severe attack of angioneurotic edema involving the face, hands, feet and arms. In addition he said that for four days he had had burning and smarting pain in the right side, and had noted the development of an eruption, which extended across the lower thorax onto the abdomen below the navel. He complained of mild general abdominal colic and anorexia of two days' duration.

Examination disclosed a hyperemic pharynx in addition to the giant urticaria and herpes zoster of the right tenth and eleventh dorsal nerves. The temperature was 99 F. The same evening the abdominal cramps became marked and were general, with no localization. There was pain and hyperesthesia of the right side of the abdomen, brought on by movement, sneezing or coughing. The abdominal pain was severe throughout the night and was slightly relieved by heat and tincture of belladonna in 8 minim (0.5 cc.) doses.

The next morning on March 29, 1929, the boy appeared quite ill. His temperature was 102.4 F. and the abdominal pain was generalized. He vomited once and had a bowel movement. The angioneurotic edema had disappeared, and pressure deep in the right lower abdominal quadrant elicited pain. Rectal examination confirmed the presence of right pelvic tenderness. Involuntary rigidity was not distinct and could not be differentiated from the hyperesthesia of the herpes zoster. The patient was hospitalized, and the white count was 19,000 with 88 per cent of polymorphonuclears. The urine was normal.

The persistent abdominal pain, rising temperature, rectal tenderness and leukocytosis, together with the disappearance of the angioneurotic edema, impressed on us the probability of a retrocecal appendicitis. At operation a ruptured retrocecal appendix was found and a moderate amount of free pus. Drainage of the pelvis and pericolic area was carried out, but the patient developed a pelvic abscess, which spontaneously cleared up. On the third day after operation fruit juices were added to the diet, with the prompt development of the angioneurotic edema. Ephedrine sulphate solution and restricted diet gave him relief in a few days. Since then it has been learned that he was sensitive to pineapple, strawberries, grapes and bananas. On May 14, he still showed the stains and marks of the herpes zoster.

The differential diagnosis was complicated by the fact that angioneurotic edema may attack the gastro-intestinal mucosa with the production of fever, colicky pains and vomiting; and herpes zoster produces hyperesthesia along the course of nerve distribution (in this case, in McBurney's region). Further, the posterior spinal ganglions from the third dorsal to the second lumbar spinal roots are in relation with the gastro-intestinal tract by sympathetic afferent fibers, hence the possibility of gastro-intestinal disturbances in herpes zoster.

DISCUSSION

DR. MAXWELL P. BOROVSKY: In a case in my service at the Cook County Contagious Hospital in which a diagnosis of scarlet fever was made and in which diphtheria was suspected, an intern discovered right rectal rigidity and tenderness. There was no vomiting, but in view of the fact that there was such a definite localization of pain and distinct tenderness over McBurney's point, it was decided

to operate for appendicitis. Before this could be done, permission to operate had to be obtained from the parents. They were called and recommended that the intern communicate with the physician who had charge of the boy before his admission to the contagious ward of the hospital. A diagnosis of scarlet fever and suspected diphtheria had been made by that physician, and he had injected 5,000 units of diphtheria antitoxin into the right lower abdominal wall. The physical manifestations of appendicitis were due to that injection.

DR. MAURICE L. BLATT: During the past winter, a young boy was admitted to the County Hospital with a condition not unlike that in the case reported by Dr. Levin. The resident physician, Dr. Hoffman, telephoned me that he had an interesting case, but did not know into which ward to send the patient. The boy had a fractured forearm. He had fallen from a bicycle, and at the moment was bitten by a dog over the point of fracture. Examinations showed that he also had chickenpox.

SEPTIC ULCERATION OF THE ESOPHAGUS IN A NEWLY BORN INFANT. Presented by DR. GERARD N. KROST.

A newly born infant, delivered normally and with an unimportant family history, had a profuse hemorrhage from the mouth at the end of forty-eight hours of life. Bleeding was controlled by injection of whole human blood. Fluids heretofore retained by mouth were regurgitated. A catheter passed into the esophagus would not pass beyond the lower end. Barium sulphate did not pass this obstruction at the end of twenty-four hours, as shown by the roentgenograms. A diagnosis of esophageal stricture and hemorrhagic disease of the new-born was made. Gastrostomy was performed on the sixth day. Fluids given by gastrostomy were regurgitated by mouth in small amounts, with some recurrence of bleeding, showing the esophagus at least slightly patent. Respiratory symptoms then manifested themselves, and death occurred on the eighth day. The temperature was never normal from the first day of life, fluctuating from 100 F. on the first day of life to 105.2 F. on the day of death.

Postmortem examination revealed a septic ulceration of the esophagus and metastatic abscesses of the lung. From the extent of the ulceration and the rapidity of the occurrence of symptoms, in less than forty-eight hours of life, the condition in the esophagus was probably congenital and the abscesses in the lung probably secondary to the condition in the esophagus, as abscesses of the lung are rare congenital infections. There was no history of infection, sore throat or influenza in the mother previous to delivery.

CONGENITAL BALLOON CYST OF THE UPPER LOBE OF THE LEFT LUNG. Presented by DR. ARTHUR H. PARMELEE.

Book Reviews

MENTAL DEFICIENCY (AMENTIA). By A. F. TREDGOLD. Price, $7.50. Pp. 512, with illustrations. New York: William Wood & Company, 1929.

This is the fifth edition of the standard English textbook on mental deficiency. We know of no other book which discusses amentia with such comprehensiveness. The clinical pictures and characteristic pathology of amentia and its legal status and social implications are described in a sane but liberal fashion. The methods of diagnosis, including the more commonly used mental tests, are given, and a form for case taking is added. The author also briefly reviews the training of the mentally deficient. His summary of the English Mental Deficiency Acts of 1913 and 1927 leads one to believe that the English have developed a legal formula which may well serve as a model for the rest of the world. The Act of 1927 breathes the spirit of the psychologist and psychiatrist. One paragraph defines the class of moral defectives as composed of "persons in whose case there exists mental defectiveness coupled with strongly vicious or criminal propensities, and who require care, supervision, and control for the protection of others." Tredgold interprets this as meaning that they are "defective in adaptiveness. . . ." This provides a legal conception by which persons incorrigibly unadapted to social life can be rendered innocuous to society.

The book reveals at every hand the work of a man who has had personal experience with the problems that he discusses. The clinical pictures and the sociologic and medicolegal discussions are, therefore, the best part. The treatment of the etiology and psychology of amentia is less valuable. It is scholastic in tone and shows an astonishing failure to glean any valuable suggestions from modern pediatrics and individual psychology. The theory of conditional reflexes finds no place. Iodine deficiency as a cause of endemic cretinism is not mentioned. The most serious shortcoming, however, is the indifferent discussion of environmental influences. Parental miseducation certainly deserves more than a cursory mention; Tredgold has underestimated its importance in stimulating asocial tendencies. In other ways, too, pediatric research of the past twenty years has been neglected, as, for instance, when the newer work on birth injuries is barely mentioned, and when spasmophilia is completely ignored while teething is given its mythical rôle in the causation of infantile convulsions. If my criticism on these points is severe, I believe it to be justified by the fact that a book of such popularity and value as Tredgold's has no right to fall behind in the march of science. It is especially inexcusable since the title page describes this edition as "largely rewritten."

HELMINTHES ET PROTOZOAIRES LES PLUS FREQUENTS. By DOCTEUR LEO. Price, 20 francs. Pp. 210. Paris: L'Expansion Scientifique Française, 1929.

The book includes a consideration of the symptomatology and treatment for diseases caused by *Ascaris lumbricoides, Oxyuris vermicularis, Trichocephalus dispar, Lamblia intestinalis* and *Trichomonas intestinalis.* There are 210 pages divided into five chapters as follows: 1, Worm Toxins; 2, Symptoms; 3, Rôle of the Laboratory; 4, Diagnosis, and 5, Treatment.

It is stated that the author wishes to present a practical work for physicians and specialists who encounter the carriers of these common parasites.

Much emphasis is laid on the toxicity of the parasites, the author stating that it must be admitted from the beginning that this toxicity of the worms causes all the signs and may be far-reaching. He further states that the "laboratory procedures for finding the ova in the stools are too useful to be passed without mention," but he believes that when the observations are negative "they should be accepted in spirit but should not take the place in diagnosis of the purely

clinical findings." Somewhat contradictory are the statements on page 93. "The analysis of the stools for the Trichocephalus is the only means of diagnosis, if it is not made clinically exclusively"; and "The Lamblia and the Trichomonas have been shown in the stools. For these two varieties, this means of diagnosis is the only possible way. These parasites are invisible to the naked eye." The general tone of the book does not conform to the accepted teachings prevalent in this country.

Thymol, carbonate of bismuth and pelletierine are the three substances in which the author places greatest reliance in the treatment for conditions caused by *Oxyuris, Trichocephalus* and *Ascaris.* Other drugs are given for conditions caused by *Lamblia* and *Trichomonas;* for the former, the arsenicals especially; for the latter, spirits of turpentine by mouth.

The author has studied the subject exhaustively, judging from the number of references contained within the pages of the book. Unfortunately, however, the subject is presented purely from the point of view of the French writers, as the references are, with few exceptions, French.

DIAGNOSTIK UND THERAPIE DER KINDERKRANKHEITEN. By PROF. DR. F. LUST. Price, 10 marks. Pp. 536. Berlin: Urban & Schwarzenberg, 1929.

This is the sixth edition of a good textbook of pediatrics. Diagnosis is stressed. A noteworthy feature is the extensive discussion of the physical and especially the mental development of the child from birth to school age. A brief outline of mentality tests for children up to 8 years is given. Care of the first teeth is urged and dentistry recommended. One sentence is worthy of translation, even in a brief review: "With the advance of pediatric knowledge, the catch-all diagnosis of 'teething' is becoming more and more unnecessary." The discussion of the various diseases is complete, extremely concise and clear. The therapy is entirely modern and conservative.

A full chapter is given over to the description of therapeutic procedures used in pediatric practice. This also is complete and includes all the more recent methods. It is delightful to have a book in which these essentials are grouped together. A second section of the book is devoted to a list of drugs and pharmaceutics with dosages.

THERAPEUTISCHES VADEMECUM FÜR DIE KINDERPRAXIS. By H. KLEINSCHMIDT. Second edition. Pp. 256. Berlin: S. Karger, 1929.

The present volume is the sixth edition of the useful handbook on therapeutics by Kleinschmidt. No attempt is made to cover each individual topic completely from the therapeutic point of view, but to give the practitioner a few of the accepted therapeutic measures. Its translation into English, Portuguese and Russian is indicative of its wide demand. It can be recommended as giving the present ideas in therapy in German clinics.

SELECTED ARTICLES. From the Department of Pediatrics University of Toronto, and the Hospital for Sick Children, Toronto. Pp. 536, with tables and illustrations.

Sixty selected articles and four reports of cases from the pediatrics department of the University of Toronto make up the volume.

Directory of Pediatric Societies

INTERNATIONAL

INTERNATIONAL CONGRESS ON PEDIATRICS

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. William Weston, 1231 Bull St., Columbia, S. C.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
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AMERICAN PEDIATRIC SOCIETY

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Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.

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SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

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Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

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Place: Miami, Fla. Time: Nov. 20-22, 1929.

LOCAL

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Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

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Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

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Secretary-Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

GEORGIA PEDIATRIC SOCIETY

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Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

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Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

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Secretary: Dr. Bert I. Beverly, 130 S. Oak Park Ave., Oak Park, Ill.
Place: City Club. Time: Third Tuesday of each month.

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Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
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Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

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President: Dr. Louis M. Ruderman, 961 Eastern Pkwy., Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Secretary: Dr. Joseph Golomb, 496 E. 175th St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
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Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

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Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

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President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

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Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

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Secretary: Dr. Carol Pounders, 110 W. 10th St., Oklahoma City.
Place: Shawnee. Time: May, 1930.

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Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

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Secretary: Dr. Armin Rembe, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

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President: Dr. A. L. Kastner, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

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President: Dr. G. A. Davis, 12 Belsize Drive, Toronto.
Secretary: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Time: November 17, December 15, February 16 and March 15.

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